World Journal of Gastroenterology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.3748/wjg.v21.i26.7988

World J Gastroenterol 2015 July 14; 21(26): 7988-8003
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

EDITORIAL

Current status and progress of pancreatic cancer in China

Quan-Jun Lin, Feng Yang, Chen Jin, De-Liang Fu

Quan-Jun Lin, Feng Yang, Chen Jin, De-Liang Fu, Department of Pancreatic Surgery, Pancreatic Disease Institute, Huashan Hospital, Shanghai Medical College, Fudan University, Shanghai 200040, China

Author contributions: Lin QJ contributed to data acquisition, drafting and revising the article, and final approval of the version to be published; Yang F contributed to the conception and design of the review, data acquisition, analysis and interpretation, revising it critically for important intellectual content and the final approval of the version to be published; Jin C and Fu DL contributed to the conception and design of the review, and final approval of it.

Supported by New Outstanding Youth Program of Shanghai Municipal Health Bureau, No. XYQ2013090; Shanghai Young Physician Training Program and the Zhuo-Xue Project of Fudan University, the National Natural Science Foundation of China, No. 81071884; Research Fund for the Doctoral Program of Higher Education of China, No. 20110071110065.

Conflict-of-interest statement: We declare no conflicts of interest.

Correspondence to: Feng Yang, Professor, Department of Pancreatic Surgery, Pancreatic Disease Institute, Huashan Hospital, Shanghai Medical College, Fudan University, 12 Central Urumqi Road, Shanghai 200040, China. yffudan98@126.com
Telephone: +86-21-52887164
Fax: +86-21-52888277

Received: January 26, 2015
Peer-review started: January 27, 2015
First decision: March 12, 2015
Revised: March 31, 2015
Accepted: April 16, 2015
Article in press: April 17, 2015
Published online: July 14, 2015

Abstract

Cancer is currently one of the most important public health problems in the world. Pancreatic cancer is a fatal disease with poor prognosis. As in most other countries, the health burden of pancreatic cancer in China is increasing, with annual mortality rates almost equal to incidence rates. The increasing trend of pancreatic cancer incidence is more significant in the rural areas than in the urban areas. Annual diagnoses and deaths of pancreatic cancer in China are now beyond the number of cases in the United States. GLOBOCAN 2012 estimates that cases in China account for 19.45% (65727/337872) of all newly diagnosed pancreatic cancer and 19.27% (63662/330391) of all deaths from pancreatic cancer worldwide. The population's growing socioeconomic status contributes to the rapid increase of China's proportional contribution to global rates. Here, we present an overview of control programs for pancreatic cancer in China focusing on prevention, early diagnosis and treatment. In addition, we describe key epidemiological, demographic, and socioeconomic differences between China and developed countries. Facts including no nationwide screening program for pancreatic cancer, delay in early detection resulting in a late stage at presentation, lack of awareness of pancreatic cancer in the Chinese population, and low investment compared with other cancer types by government have led to backwardness in China's pancreatic cancer diagnosis and treatment. Finally, we suggest measures to improve health outcomes of pancreatic cancer patients in China.

Key words: Pancreatic cancer; Incidence; Diagnosis; Treatment

Core tip: The health burden of pancreatic cancer in China is increasing, with annual mortality rates almost equal to incidence rates. Cases in China account for 19.45% of all newly diagnosed pancreatic cancer and 19.27% of all deaths from pancreatic cancer worldwide.

Facts including no nationwide screening program for pancreatic cancer, delay in early detection resulting in a late stage at presentation, lack of awareness of pancreatic cancer in the Chinese population, and low investment compared with other cancer types by government have led to backwardness of China's pancreatic cancer diagnosis and treatment.

Lin QJ, Yang F, Jin C, Fu DL. Current status and progress of pancreatic cancer in China. *World J Gastroenterol* 2015; 21(26): 7988-8003 Available from: URL: http://www.wjgnet.com/1007-9327/full/v21/i26/7988.htm DOI: http://dx.doi.org/10.3748/wjg.v21.i26.7988

WORLDWIDE EPIDEMIOLOGY OF PANCREATIC CANCER

Pancreatic cancer, one of the most frequent cancers in the world, is a devastating malignant disease with a median survival of 3-6 mo and a 5-year survival rate of less than 5%[1-4]. Despite improvements in surgical techniques and adjuvant medical therapy, these figures have not changed in over four decades, with the mortality approaching the incidence. According to the latest global estimation, GLOBOCAN 2012, the age standardized rate (ASR) of pancreatic cancer incidence data is 4.9 per 100000 in men, and 3.6 per 100000 in women. ASR mortality rate is 4.7 per 100000 in men, and 3.4 per 100000 in women. Worldwide, the age-standardized rate (ASR-W) for the incidence and mortality of pancreatic cancer is 4.2% (Figure 1) and 4.0% (Figure 2), respectively[5]. In the United States, the ASR incidence and mortality of pancreatic cancer is 7.5% and 7.0%, respectively. The recent data showed that 48960 people were estimated to be diagnosed with pancreatic cancer in 2015, and 40560 people would die from pancreatic cancer in the United States[6].

Epidemiology in China

China is the largest developing country with nearly a fifth of the global population. As a result of rapid urbanization, more and more Chinese people live in urban areas. Combined with other factors such as aging and environmental pollution, the disease spectrum in China has shifted from infectious to non-infectious diseases. Among the non-communicable diseases, the health burden of cancer is increasing. Although China has a lower incidence of pancreatic cancer than western countries, the incidence of this disease in China has increased as fast as that worldwide recently. In 2010, 34509 men and 23226 women died from pancreatic cancer in China, with the number of deaths exceeding that in the United States[5,7,8].

Significant improvements of pancreatic cancer diagnosis and treatment have been achieved by China over the past 30 years. Here, we review the status of pancreatic cancer in China, and describe important epidemiological, risk factors, screening methods, diagnosis and therapy of pancreatic cancer. In addition, we discuss the challenges and trends of pancreatic cancer in China, and explore development of a multicenter cooperative research system to improve its clinical outcome.

Incidence and mortality

Population-based cancer registries collect data on annual cancer incidence and mortality to provide accurate and up-to-date information that is vital for cancer prevention, control, and research[7]. Since 2006, data contained in the Cancer Registry Annual Report released by the National Central Cancer Registry (NCCR) indicate that the incidence and mortality of pancreatic cancer in China has gradually risen[9]. Although the number of cancer registries in China is increasing, the available data for incidence and mortality of pancreatic cancer covers only about 13% of the nation's population, while nearly 100% of the population in the United States is covered[6,10]. Currently, the true burden of pancreatic cancer in China cannot be estimated by using data from the Cancer Registry Annual Report alone, due to the above limitation. Thus, expansion of cancer registries covering more population would improve accuracy of estimates of cancer burden.

Incidence

GLOBOCAN 2012 estimated that pancreatic cancer was one of the most frequent malignancies in China, with an ASR-W incidence of 3.6 per 100000 for both sexes[5]. According to the Chinese Cancer Registry Annual Report 2012, the incidence of pancreatic cancer fluctuated according to sex, region and age. The crude incidence rate of pancreatic cancer in registration areas was 7.28 per 100000, with 8.24 per 100000 for men and 6.29 per 100000 for women in 2009. The ASR was 3.35 per 100000 with 4.01 and 2.72 per 100000 for men and women, respectively[10].

The crude incidence rate of pancreatic cancer in Chinese urban populations was 8.19 per 100000 (9.36 per 100000 for men and 7.00 per 100000 for women), which was 51.39% higher than that in rural areas (5.41 per 100000 overall; 5.97 per 100000 for men and 4.83 per 100000 for women). The data remained 27.76% higher after age standardization[10]. Standardized by the age structures worldwide, the ASR incidence in urban areas was 4.96 per 100000, which was also higher than that in rural areas (3.83 per 100000). Among the urban cancer registration areas, Shanghai had the highest crude incidence rate of 15.19 per 100000 (Figure 3).

The age-specific incidence rates of pancreatic cancer dramatically increased after 40 years old in

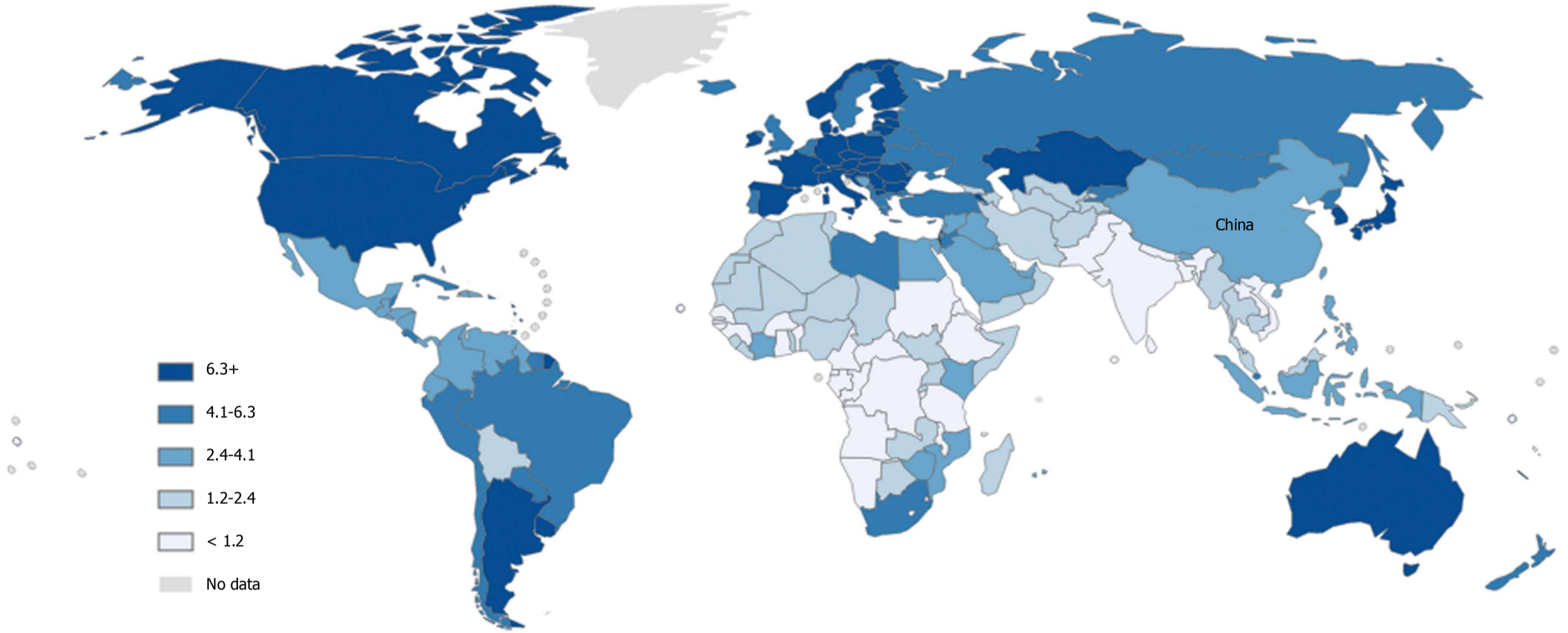

Figure 1 Map of estimated global pancreatic cancer incidence rates according to GLOBOCAN 2012.

China, with the incidence peak at about 80 years old (Figure 4). The trends in urban and rural areas were similar to those in the entire country, with the age-specific incidence rate in urban areas higher than that in rural areas after age 50 years. The cumulative incidence rate for patients aged 0-64 years was 0.21%, while for those aged 0-74 years it was 0.54%[10]. Comparison of age distribution among some major countries and continents showed that more patients younger than 65 years were diagnosed with pancreatic cancer in China, which means that age at diagnosis of pancreatic cancer in China is less than that in western countries (Figure 5). In China, 61.2% of patients with pancreatic cancer were aged 65 years or older, compared with 80.1% of patients in Japan.

Although there were fluctuations according to sex and region, the upward trend in the incidence rate of pancreatic cancer is real in China. According to the Chinese NCCR, the incidence rate increased from 6.26 per 100000 in 2003 to 8.37 per 100000 in 2009[11]. During this 7-year period, the incidence rate increased from 6.83 to 9.48 per 100000 in men and from 5.67 to 7.24 per 100000 in women. The increasing trend of pancreatic cancer incidence was more significant in rural than in urban areas. The incidence rate increased 1.27 times from 2003 to 2009 in urban areas, while the rate was 1.61 times higher in 2009 than in 2003 in rural areas.

Mortality

Pancreatic cancer is a rapidly disastrous malignancy with dismal prognosis. Recent mortality rates of pancreatic cancer in developed countries such as Japan have

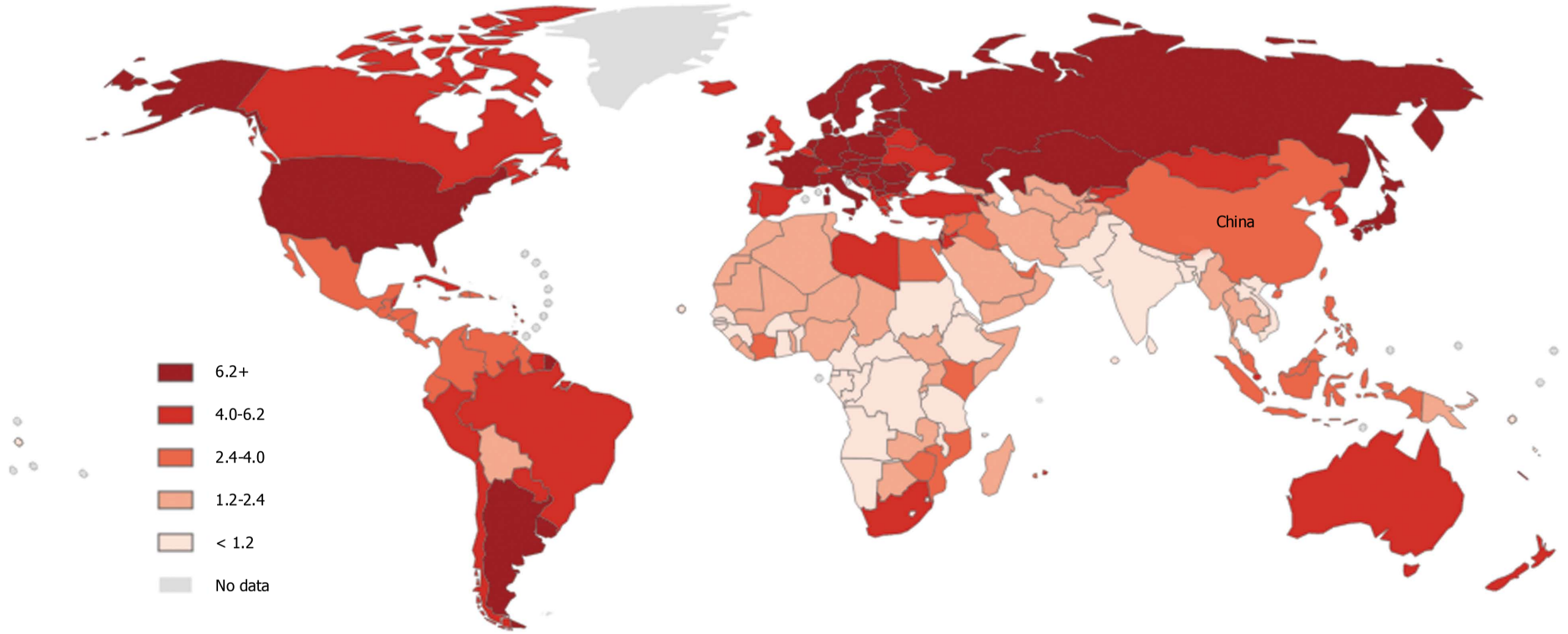

Figure 2 Map of estimated global pancreatic cancer mortality rates according to GLOBOCAN 2012.

stabilized after an increase[12], while in China mortality due to pancreatic cancer is rising. Despite that, the prevalence, incidence and mortality of pancreatic cancer in China are relatively lower than those in developed countries such as Europe, the United States and Japan, and comparison of mortality-to-prevalence ratios showed that survival outcome for pancreatic cancer is worse in China than in most other countries. The mortality-to-prevalence ratio amounts to 0.85 in China, compared with 0.7 in the United States, 0.56 in South Korea, 0.55 in Germany, and 0.4 in Japan (Figure 6). The phenomenon may be due to lack of improvement in the treatment of pancreatic cancer, especially in China[13].

According to the Cancer Registry Annual Report 2012, pancreatic cancer ranks as the seventh highest cause of cancer death in China, with a crude mortality of 6.61 per 100000. The mortality rate in urban areas (7.42 per 100000) was 50.20% higher than that in rural areas (4.94 per 100000). The data remained 27.09% higher after age standardization. The trend might be due to disparities in socioeconomic circumstance, and lifestyle between urban and rural areas. The mortality reached the peak at around 80 years old in both urban and rural areas (Figure 7), which was similar to the incidence. From 2003 to 2009, the mortality rate of pancreatic cancer increased from 5.63 to 7.78 per 100000[11]. The upward trend in mortality concerns both men and women, and both urban and rural areas.

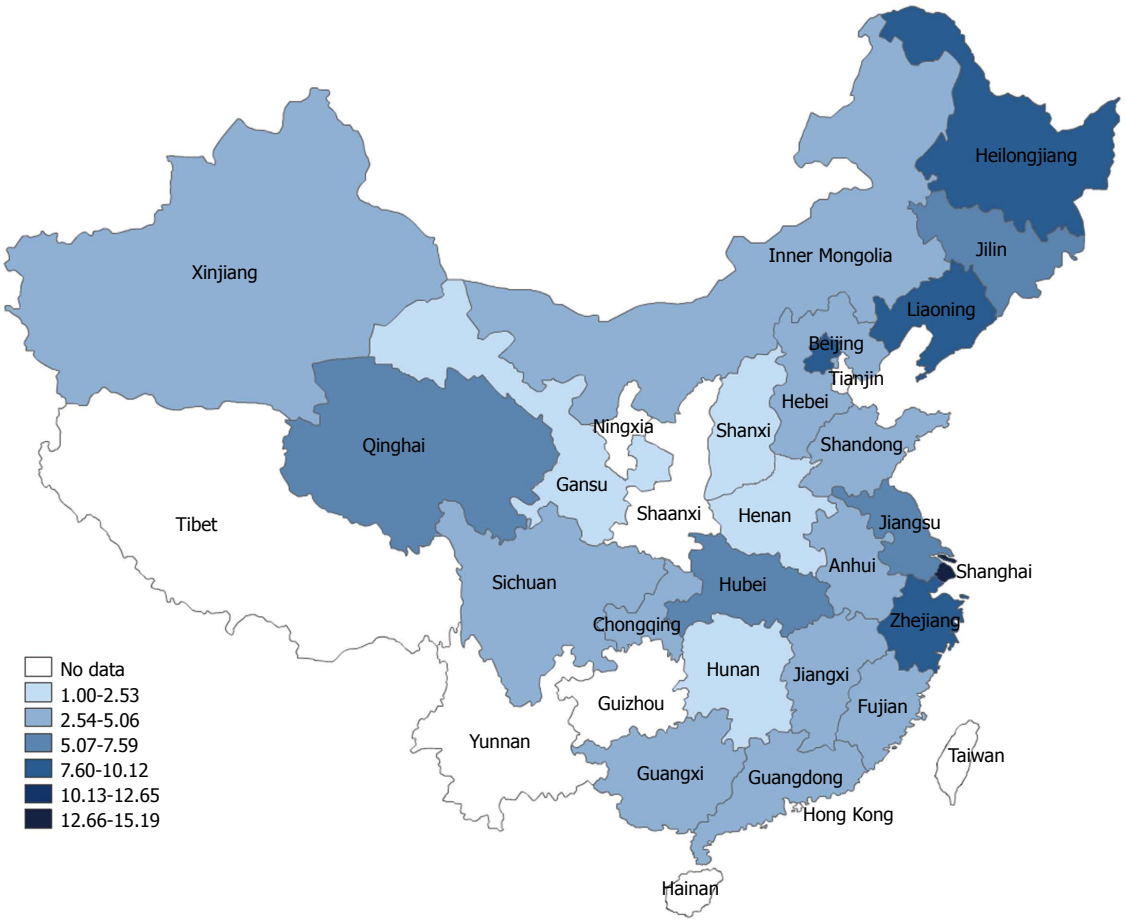

Figure 3 Crude rate (1/10^5) of pancreatic cancer in China. Figure based on data from the Chinese Cancer Registry annual report (2012).

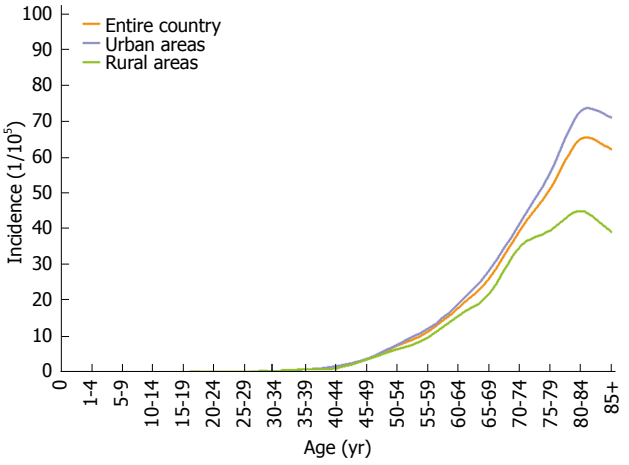

Figure 4 Age-specific incidence of pancreatic cancer in China, 2009. Figure based on data from the Chinese Cancer Registry annual report.

RISK FACTORS OF PANCREATIC CANCER

Pancreatic cancer is considered a malignancy correlated with industrialization as suggested by the fact that the majority of deaths occurred in developed countries. Despite the fact that it is unclear what factors cause pancreatic cancer, several risk factors and established genetic syndromes are associated with pancreatic cancer. Although identification of country-specific trends for risk of pancreatic cancer is valuable, risk factors in China are similar to those worldwide. Recent substantial increases in the prevalence of cigarette smoking, obesity, and diabetes mellitus in China may be related to the increasing incidence of pancreatic cancer. Also, studies show that severe deterioration of the environment in China and problems with food contamination may contribute to the increasing occurrence of cancer[14,15].

Tobacco use

Tobacco use is one of the most important risk factors of pancreatic cancer, and a dose- and duration-related pattern has been demonstrated for earlier age of onset[16,17]. Around the world, 9% of all cancer deaths are related to smoking among male smokers, and male smokers have a 74% higher risk of pancreatic cancer compared with non-smokers[18]. A recent hospital-based case-control study by Wang *et al*[19] showed that current smokers had a significantly increased risk of pancreatic cancer (OR = 1.71, 95%CI: 1.25-2.35) with a decreasing trend in risk correlated with years of smoking cessation. Another case-control study

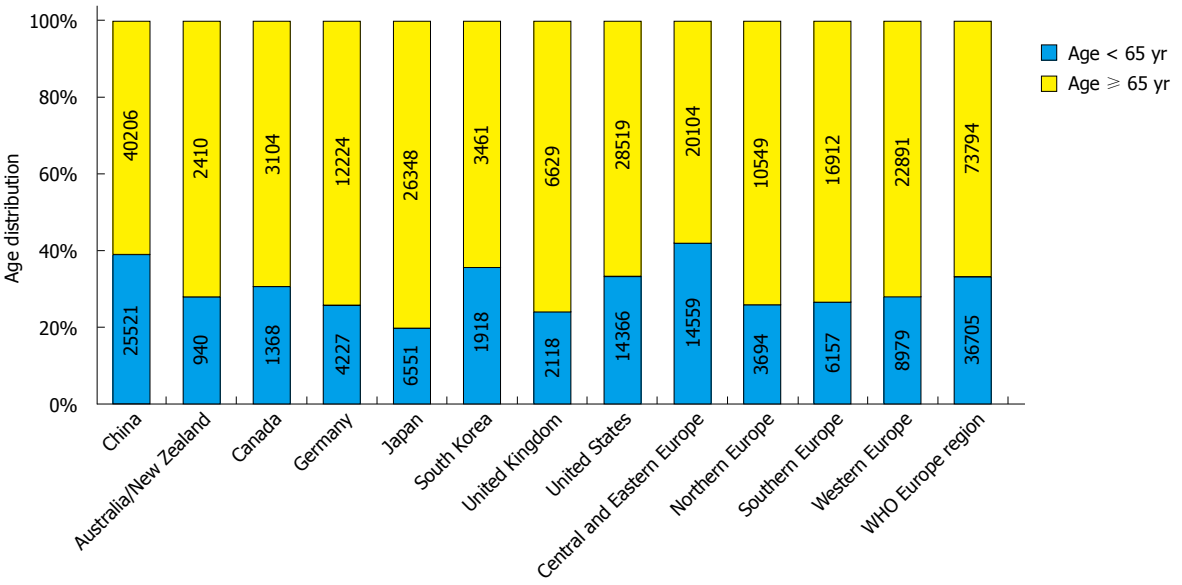

Figure 5 Comparison of age distribution of patients with pancreatic cancer between China and some major countries and continents.

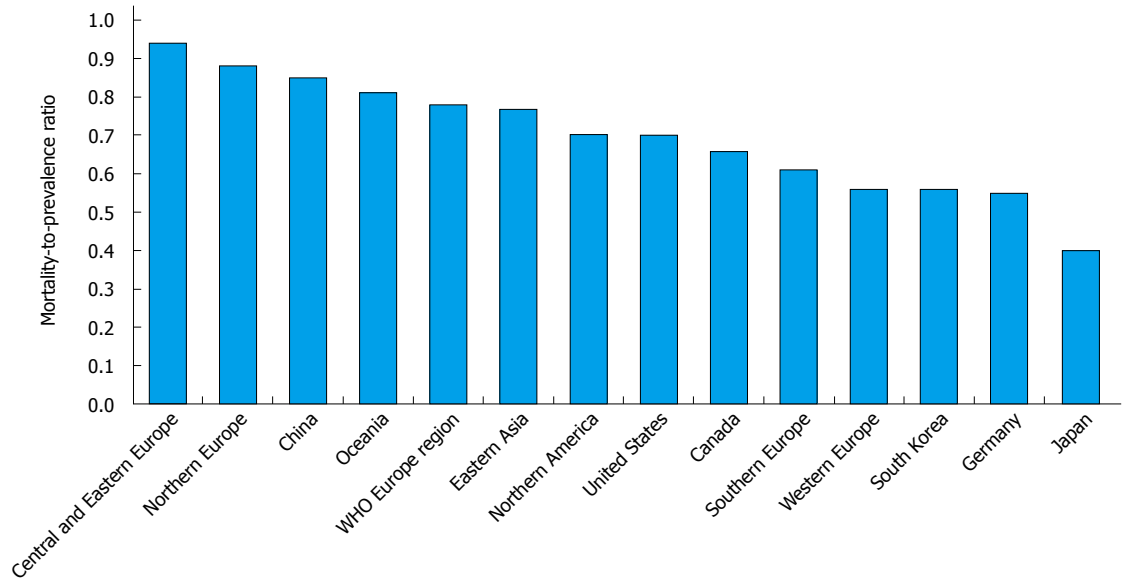

Figure 6 Comparison of mortality-to-prevalence ratio of pancreatic cancer between China and some major countries and continents.

by Yin *et al*[20] revealed that smokers had an OR for pancreatic cancer of 3.53 (95%CI: 3.0-9.6) compared with non-smokers, and smoking in the morning was an increased risk factor for pancreatic cancer (OR = 5.50, 95%CI: 1.22-24.81). In addition, secondhand smoke exposure may increase the risk of pancreatic cancer by 50%, and children exposed passively to tobacco smoke have a double risk of pancreatic cancer as adults[21,22].

Obesity and dietary factors

Obesity, which is associated with increased risk of diabetes mellitus, is also a risk factor for the development of pancreatic cancer[23]. A case-control study including 841 patients with pancreatic adenocarcinoma and 754 healthy individuals showed that being overweight [body mass index (BMI) of 25-29.9] or obese (BMI ⩾ 30) during early adulthood was associated with an increased risk of pancreatic cancer. A younger age of disease onset and obesity at an older age reduced overall survival in patients with pancreatic cancer, regardless of disease stage or tumor resection status[24]. Studies have shown that the relative risk of pancreatic cancer was 1.16 in men and 1.10 in women per 5-point increase in BMI[25,26].

Dietary factors are also related to pancreatic cancer. Although there is evidence that folate and folate-containing foods exert a protective effect against pancreatic cancer[27], this was not confirmed in a recent study[28]. A multicenter case-control study by Chinese researchers[29] showed that reduced vegetable consumption was significantly associated with pan-

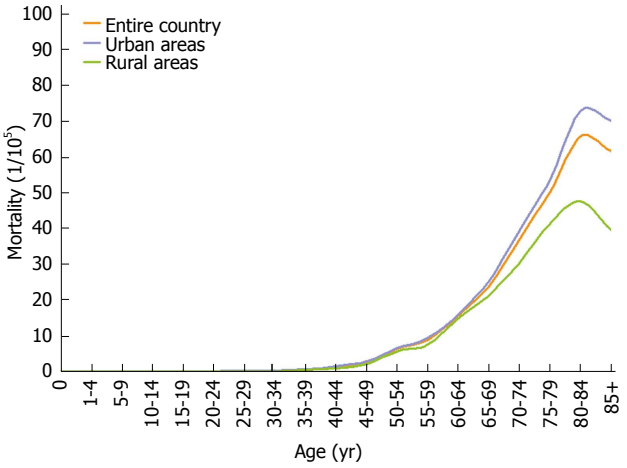

Figure 7 Age-specific mortality of pancreatic cancer in China, 2009. Figure based on data from the Chinese Cancer Registry annual report.

creatic cancer (*P* trend 0.04), and meat and fruit consumption was not significantly related to the risk of pancreatic cancer. A protective effect was discovered for fruit (OR = 1.73 for consumption of 1 or 2 times per week *vs* > 3 times per week; 95%CI: 1.05-2.86). A population-based case-control study from an urban area of Shanghai[30] reported that dietary energy density (defined as the amount of energy theoretically able to be metabolized per unit weight of food) had an OR for pancreatic cancer of 1.16 per unit increase (95%CI: 1.07-1.27), and dietary energy density was positively related to risk of pancreatic cancer. The molecular mechanisms to explain these results are not well investigated, but chronic inflammation mediated by secreted molecules from adipose tissue and hormonal factors is likely involved[24,31]. Supporting this hypothesis, a study by Zhang *et al*[32] showed that dietary and other lifestyle factors that influenced insulin resistance were also associated with the risk of pancreatic cancer.

Diabetes

Whether diabetes mellitus is a risk factor or a result of pancreatic cancer is still unclear. However, diabetes mellitus improves following pancreatectomy, suggesting that diabetes mellitus may be caused by pancreatic cancer. Studies have shown that 25% of patients diagnosed with pancreatic cancer had diabetes mellitus, among whom 40% were pre-diabetic[33,34]. The association between diabetes mellitus and pancreatic cancer has been summarized in several meta-analyses[35-37]. A study by Huxley *et al*[36] reported that the overall risk was 1.82 (95%CI: 1.66-1.89) for developing pancreatic cancer in patients with diabetes mellitus, relative to patients without diabetes mellitus. The risk of pancreatic cancer declines with increased duration of diabetes mellitus. Patients with diabetes mellitus within 4 years had a 50% increased risk of pancreatic cancer compared with patients with diabetes mellitus for 5 years or longer. Patients whose diabetes mellitus had lasted 5 years or longer had a 50% greater relative risk than those without diabetes mellitus[36]. This is not surprising because pancreatic-cancer-associated diabetes mellitus is predominantly new onset[38]. In a Chinese retrospective cohort study, male and female patients with type 2 diabetes mellitus were 2.97 and 2.68 times more likely, respectively, to develop pancreatic cancer compared with the general population[39]. Similar results were obtained by Kuang and coworkers[40], who showed that the incidence of diabetes mellitus was higher in pancreatic cancer patients than in controls.

Genetic risk factors

Although the occurrence of pancreatic cancer seems to be sporadic, it has been reported that 5%-10% of pancreatic cancer patients have hereditary factors[41]. Cases of inherited predisposition to pancreatic cancer fall roughly into three categories[23]. The first consists of hereditary cancer syndromes such as Lynch syndrome[42], familial adenomatous polyposis, Peutz-Jeghers syndrome, and familial atypical multiple mole melanoma syndrome, which are characterized by specific germ-line gene mutations and associated with increased risks of pancreatic cancer. The second category comprises conditions such as hereditary pancreatitis and cystic fibrosis, in which there is an inherited predisposition to the development of pancreatic cancer. The third category is familial pancreatic cancer, defined as two or more first-degree relatives with pancreatic cancer that does not fulfill the criteria of other hereditary cancer syndromes with increased risks of pancreatic cancer[43].

Other risk factors

Additional risk factors including male sex, low income, advanced age, alcohol use[40], chronic pancreatitis[44], a history of cholecystectomy or partial gastrectomy[45,46], and chronic infections have also been shown associated with pancreatic cancer[47]. Moreover, it has been reported that some pancreatic cystic lesions such as intraductal papillary mucinous neoplasm and mucinous cystic neoplasm have the potential to progress to invasive pancreatic cancer[48], and patients with these lesions belong to groups at high risk of pancreatic cancer. In addition to the above risk factors, other factors such as environmental pollution and food contamination, which are becoming serious issues affecting public health in China[49], may be associated with the increased trend of pancreatic cancer. Although so far these associations lack solid epidemiological evidence, a recent cohort study demonstrated that airborne particulate matter of diameter < 10 μm from the incinerator was associated with pancreatic cancer mortality[50].

SCREENING FOR EARLY PANCREATIC CANCER

Recent studies suggest that pancreatic cancer develops over a long time with an average of nearly 17 years from cancer-initiating cells to metastatic cancer subclones, followed by death after approximately 2.7 years[51,52]. Patients with small tumors detected at early stages have reportedly better outcomes[53-55]. Thus, a screening program for high-risk individuals has the benefit of better outcomes in patients with pancreatic cancer.

There is no nationwide screening program for pancreatic cancer in China at present. Obstacles to implementation of a population-based screening program include insufficient convincing accuracy and cost-effectiveness data; insufficient equipment; and inadequate insurance coverage for such a screening program. There has been no consensus on the definition of high-risk individuals for pancreatic cancer until now. Patients in China who are at high risk of pancreatic cancer may be characterized by any of the following[56,57]: (1) older than 40 years and presenting with nonspecific abdominal symptoms; (2) a family history of pancreatic cancer; (3) new-onset diabetes mellitus, especially in those older than 60 years with either atypical diabetes mellitus or rapidly developing insulin resistance, without family history or obesity; (4) chronic pancreatitis, especially when accompanied by precancerous lesions; (5) intraductal papillary mucinous neoplasms; (6) familial adenomatous polyposis; (7) distal subtotal gastrectomy for benign disease, especially 20 years after resection; and (8) heavy tobacco or alcohol use or long-term contact with hazardous chemical substances.

When encountering these populations, non-invasive screening methods such as ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography (MRCP), combined with pancreatic-cancer-related biomarker examination are recommended. Among these high-risk groups, patients with new-onset diabetes mellitus may be an attractive screening target for early pancreatic cancer. The potential clinical benefit of screening for early pancreatic cancer in high-risk groups appears to exceed that for breast cancer[58].

Imaging

The screening modalities applied for detection of pancreatic cancer mainly include ultrasonography, CT, MRI, MRCP, and endoscopic ultrasound (EUS). Ultrasonography, a noninvasive and cost-effective modality, is frequently the first-line screening tool for patients with suspected pancreatic lesions, although it is not a reliable method, and highly dependent on the operator's experience and body habitus of patients[59]. Contrast-enhanced CT is now the worldwide imaging modality of choice for evaluation of pancreatic disease, and may be the best modality to assess resectability of pancreatic cancer[60]. Nevertheless, radiation exposure and the suboptimal detection rate limit its use as a routine screening tool for asymptomatic high-risk individuals[61]. Studies revealed that MRI and EUS may be better than CT for early diagnosis of pancreatic neoplasms[62]. Thus, it has been proposed that initial screening should include EUS with or without MRI or MRCP, but not CT or endoscopic retrograde cholangiopancreatography (ERCP)[61]. However, the high cost and limited availability of MRI generally mean that it is utilized only after ultrasonography or CT. While EUS has been used as a principal imaging modality for screening pancreatic cancer in multiple international programs[58], a study by Long *et al*[63] showed that in Shanghai only 5.7% of patients underwent EUS to detect pancreatic cancer. Evaluation of the results of EUS is dependent on the doctor's experience[64]. It is not widely used in China, and is only regularly performed in a few large medical centers[65].

Molecular markers

A limitation of screening for early pancreatic cancer is the absence of sensitive and specific markers. Compared with unwarranted imaging or more invasive testing, serological markers are always preferred due to the ease of collection, a relatively noninvasive trait. Carbohydrate antigen (CA)19-9, the only currently predictive biomarker for therapeutic outcome of pancreatic cancer, is commonly used to screen the disease. However, given the low incidence of pancreatic cancer, a blood-based marker with high specificity (99%) and sensitivity (100%) will lead to 83 false-positive for every true-positive case based on the incidence rate of 12.1 per 100000 in the United States[66]. Therefore, poor-to-moderate sensitivity and specificity in detecting pancreatic cancer limit its use in screening. For example, according to a study from China, the sensitivity of CA19-9 was only 57%, with an accuracy of 67.7%. These results indicated the limited value of CA19-9 in detecting early pancreatic cancer[67].

DIAGNOSIS

Cancer stage at diagnosis is an important factor influencing survival of pancreatic cancer patients. A multicenter nationwide study in China showed that 18.4% of pancreatic cancer patients received diagnoses at stages Ⅰ or Ⅱ, and 81.6% at stages Ⅲ or Ⅳ[68]. A recent study that included 11672 cases recorded in the Shanghai Cancer Registry 2004-2009[69] reported that nearly 42.9% of patients had regional or distant metastasis at diagnosis, whereas 49.2% had localized disease. The median survival was 3.9 mo (95%CI: 3.8-4.0 mo) and the overall 5-year survival rate was 4.1%. Reasons for poor survival of the cohort in that study included delayed diagnosis of pancreatic cancer. In contrast, the United States is better than

China at early detection of pancreatic cancer. In a recent study, Yu *et al*[70] analyzed 13131 patients with pancreatic ductal adenocarcinoma between 2004 and 2011 in the National Cancer Institute Surveillance, Epidemiology and End Results (SEER) database, which was considered representative of the United States population. They found that 62.9% of pancreatic cancer patients received diagnosis at stages Ⅰ or Ⅱ, and 37.1% at stages Ⅲ or Ⅳ. Since pancreatic cancer has no distinctive symptoms, it is usually diagnosed when a patient has symptoms of abdominal pain or jaundice. Most patients diagnosed with pancreatic cancer lack the chance of radical surgery due to late stage. It is important to determine the resectability of pancreatic cancer because the rate of postoperative complications after pancreatic surgery is high even in high-volume medical centers[71-73]. Radiological imaging is an important method for initial detection, staging, and evaluation of pancreatic cancer resectability, which includes identification of the primary tumor, local lesion resectability, and distant metastasis[59].

Multidetector row computed tomography (MDCT) is a worldwide imaging modality for evaluation of pancreatic cancer. More than 75% of patients who received a diagnosis of pancreatic cancer in China had undergone MDCT[63]. MDCT has good spatial and temporal resolution with anatomical coverage[74]. MDCT can assess both local tumor resectability and distant metastasis. It is also the best imaging modality for assessment of vascular involvement, which is crucial for prediction of tumor resectability[75,76]. MRI is also currently used for patients with pancreatic diseases[77]. Compared with CT, MRI is not only an outstanding tool for characterizing pancreatic mass, but also a successful technique for noninvasively delineating the pancreatic ductal system, as an alternative to ERCP. Positron emission tomography (PET)/CT is useful for detecting pancreatic cancer, especially metastases throughout the body[78,79]. However, widespread application of PET/CT is limited in China by its high rate of false-positive results, low spatial resolution, and high cost[80,81].

Expert for MDCT, other imaging modalities such as MRI and PET/CT are not widely used in Chinese patients[63]. In western countries, EUS has been widely used for detection of pancreatic cancer in recent years[82], especially for high-risk groups and patients with small tumors[58]. Furthermore, EUS-guided fine-needle aspiration (FNA) has the unique ability to acquire specimens for histopathological diagnosis of this devastating disease, especially in unresectable patients. A most recent study by Ngamruengphong *et al*[82], using the SEER-Medicare data including 2034 patients with pancreatic cancer, showed that preoperative EUS-FNA did not impair survival of pancreatic cancer. However, EUS-FNA is not widely performed in China, although it is now the standard of care in western countries. Less than 40% of cases diagnosed with pancreatic cancer in China had histological verification, mostly *via* surgery with pathological diagnosis[63]. Limited application of EUS in China may explain why so many patients diagnosed with unresectable pancreatic cancer lack histological confirmation.

THERAPY

Fewer than 20% of patients are eligible for curative resection as pancreatic cancer is usually detected at a late stage. Surgical resection is the cornerstone of treatment, which offers the only chance to cure patients with pancreatic cancer. Many patients have disease recurrence even after radical surgery. Adjuvant chemotherapy, radiotherapy, targeted therapy, and traditional Chinese medicine have been commonly used to improve quality of life.

Surgery

Surgical resection is the only potentially curative therapy for pancreatic cancer. Assessment of the involvement of local vessels is the key to determine tumor resectability. With improvements in safety of pancreatic surgery in recent decades, in the hope of improving long-term survival, surgeons have continued to explore the role of more extensive surgery. Whether patients should receive extended lymphadenectomy or not is controversial. A meta-analysis comparing standard lymphadenectomy with extended lymphadenectomy during pancreaticoduodenectomy for pancreatic cancer revealed that the extended procedure did not benefit overall survival, and might even cause a trend towards increased morbidity[83]. Due to no benefit in long-term survival being demonstrated, standard pancreaticoduodenectomy continues to be the choice for pancreatic head cancer.

A noteworthy change in pancreatic surgery in China may be towards a minimally invasive approach, particularly distal pancreatectomy, which could gain wide acceptance for benign and low-malignancy tumors[84,85]. A recent meta-analysis reported that laparoscopic distal pancreatectomy resulted in less loss of blood and time in hospital, and lower rates of overall complications and infections, but did not lower rates of postoperative pancreatic fistula or mortality[86]. Application of robotic surgery has advantages over laparoscopy, including the rate of R0 resections (*i.e.*, complete resection with no tumor within 1 mm of the resection margins), and greater lymph node yield[87]. A more recent study from Mayo Clinic showed that total laparoscopic pancreaticoduodenectomy (TLPD, n = 108) was feasible in the setting of pancreatic ductal adenocarcinoma, and had advantages over open pancreaticoduodenectomy (OPD), including shorter hospitalization and faster recovery, allowing patients to recover in a timelier manner and pursue adjuvant therapy. There was also a significantly longer progression-free survival in the TLPD group than in the OPD group (n = 214), while the overall survival rates of the two groups were similar[88]. Despite this, robotic

pancreatectomy is now not a common procedure in China, mainly due to cost pressures. Nevertheless, the effects and benefits need to be confirmed by more data in China.

Chemotherapy and targeted therapy

Chemotherapy for patients presenting with advanced pancreatic cancer is widespread in China. Gemcitabine is the gold standard for pancreatic cancer treatment and achieves a modest improvement in overall survival. Gemcitabine-based combination chemotherapy has been first-line for advanced pancreatic cancer for more than one decade and shows a superior clinical response and survival. In a study by Long *et al*[63], more than 30% of 846 pancreatic cancer patients recruited in a population-based study underwent chemotherapy, and 9.6% of patients received combination therapy. Regional intra-arterial infusion chemotherapy for pancreatic cancer has been safely used to suppress tumor growth and was more effective in reducing incidence of liver metastasis[89]. In a study by Jin *et al*[89], 50 patients who underwent regional intra-arterial infusion chemotherapy had disease-free and median survival times of 15.5 and 18 mo, respectively. However, the necessity for regional arterial chemotherapy remains controversial due to its invasive nature[90].

Gemcitabine plus nab-paclitaxel and FOLFIRINOX (oxaliplatin, irinotecan, fluorouracil, and leucovorin) have been recently reported to improve survival for metastatic pancreatic cancer significantly[91,92]. However, these two regimens are currently not popular in China due to increased toxicity and high cost not covered by insurance. The situation is similar for S-1, which is not inferior to gemcitabine for survival rate, with acceptable tolerance for locally advanced and metastatic pancreatic cancer[93]. Only small clinical studies have been conducted to evaluate these regimens for Chinese patients with advanced pancreatic cancer[94,95].

Targeted therapy may be promising to improve survival in advanced pancreatic cancer[96]. However, targeted therapy in several phase Ⅲ trials was not superior to standard chemotherapy[97-99]. Additionally, drug reimbursement policies strongly affect the availability of systemic therapy in China. Most targeted agents are not covered by insurance, leading to prohibitively high cost for patients and limitation of options for advanced pancreatic cancer.

Radiotherapy

The use of radiotherapy for pancreatic cancer is not popular in China. For instance, in Shanghai, only 3.5% of patients received radiotherapy as part of their primary treatment[63]. In a study by Chen *et al*[67] of pancreatic ductal adenocarcinoma, among 565 patients, only 14 underwent postoperative radiotherapy. The proportion of pancreatic cancer patients receiving radiotherapy in China is less than that in the United States. In a study by Mellon *et al*[100] using the SEER database including 2966 patients between 2004 and 2008, 62.1% of patients with pancreatic cancer received postoperative radiotherapy and had an associated survival benefit. However, similar to the incidence of new-onset pancreatic cancer in China, use of radiotherapy is also increasing. Given that patients who underwent concurrent chemoradiotherapy had better long-term survival compared with radiotherapy alone or chemotherapy alone[101], the efficacy of combination of S-1 with gemcitabine followed by concurrent radiotherapy has been investigated and appeared promising in Chinese patients with locally advanced pancreatic cancer[102]. Among the 32 patients who completed the scheduled course of chemotherapy, 30 received chemoradiotherapy. The median overall and progression-free survival was 15.2 and 9.3 mo, respectively. The 1-year and 2-year survival rates were 75% and 34.4%, respectively.

Traditional Chinese medicine

Traditional Chinese medicine, which mainly uses combinations of herbs, represents about 40% of the pharmaceutical market in China. Moreover, about 90% of oncologists prescribe herbs and 80% of patients with cancer have taken traditional Chinese medicine[103]. The widespread application of traditional Chinese medicine may be related to the belief that it can improve immune function and quality of life in cancer patients[104]. Huachansu injection, which is a water-soluble preparation made from skin of *Bufo gargarizans*, has been used in China for pancreatic cancer treatment. However, a recent randomized phase Ⅱ clinical trial showed that huachansu plus gemcitabine did not improve survival of patients with locally advanced or metastatic pancreatic cancer[105]. Turmeric root has been used medicinally for thousands of years in China. The active component is thought to be curcumin, which is commonly available worldwide and has been shown to exert activity against various malignancies, including pancreatic cancer[106]. In a phase Ⅱ study including 25 patients, curcumin showed clinical biological activity in some patients with advanced pancreatic cancer, without toxicity[107]. Another phase Ⅰ/Ⅱ study of 21 patients showed that patients with gemcitabine-resistant pancreatic cancer who received combination therapy using 8 g/d oral curcumin with gemcitabine-based chemotherapy had a median survival of 161 d (95%CI: 109-223 d) and the 1-year survival rate was 19%[108]. However, poor absorption limits the clinical activity of oral curcumin. To enhance curcumin absorption, nanotechnology and liposome-encapsulated curcumin have been studied *in vitro* and *in vivo* for pancreatic cancer[109,110].

PANCREATIC CANCER RESEARCH IN CHINA

Scientific publications related to pancreatic cancer

Table 1 Number of pancreatic cancer related publications and clinical trials by country

	China	Japan	South Korea	United Kingdom	United States	Germany
Total No. of publications[1]	3444	8126	1080	2431	16859	3650
Clinical trials published in PubMed[1]	84	400	69	153	825	227
Clinical trials ongoing[2]						
Clinicaltrials.gov	45	40	63	82	1105	122
ISRCTN	0	0	0	18	0	14
ICTRP	30	224	29	56	519	92
UMIN-CTR	0	237	0	0	0	0

[1]Retrieved from PubMed (Oct 26, 2014) with medical subject heading "pancreatic cancer" in "all fields" and "country" in "all fields" not in "text word". [2]Retrieved from Clinicaltrials.gov, ISRCTN, International Clinical Trials Registry Platform (ICTRP), and UMIN Clinical Trials Registry (UMIN-CTR), which are all approved by the International Committee of Medical Journal Editors (Oct 26, 2014) with search term "pancreatic cancer" and "country".

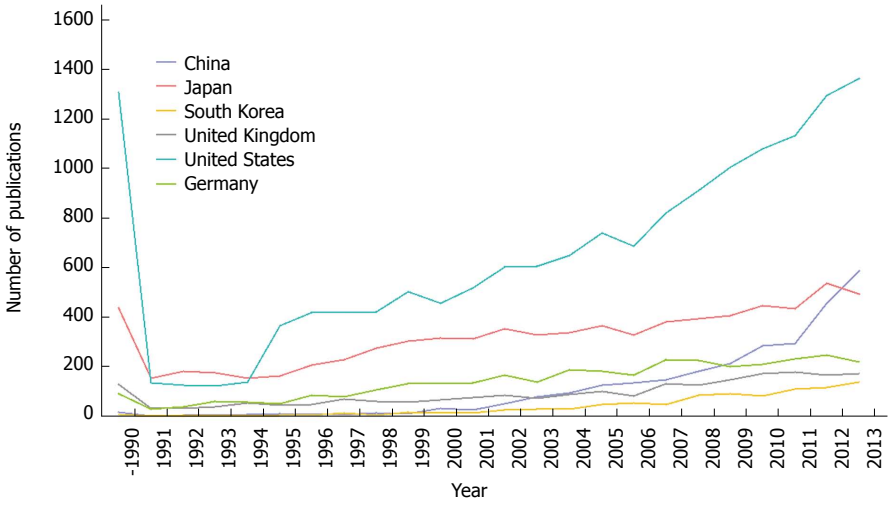

Figure 8 Publications by country in progress for pancreatic cancer over time.

from China have rapidly grown since 2007, regardless of the fact that the total number of publications in China is far less than that in the United States (Table 1). The number of publications from China in 2013 exceeded that from Japan, and was second only to the United States (Figure 8). Such great development of pancreatic cancer research in China may benefit from a steady increase in funding from the Chinese government, among which the National Nature Science Foundation of China (NSFC) is one of the most important research funds. Funding for pancreatic-cancer-related research from NSFC has steadily increased. However, investment in different cancer types remains uneven. Funding for research related to pancreatic cancer is less than for other cancer types, such as liver, breast and gastric cancers. The proportion of investment in research funding for pancreatic cancer has not been growing in the field of oncology in the past two decades (Figure 9). Nevertheless, concurrent with the rapid growth in scientific papers published from China, there is a rising concern that many of them are of inferior quality.

High-quality clinical trials are imperative for clinical decision making for care of pancreatic cancer patients. As a consequence of research funding shortage, there are only 84 clinical trials published in Pubmed and currently 75 clinical trials for pancreatic cancer registered in China (Table 1), with the numbers far less than those in developed countries. This may explain the inadequacy of high-quality pancreatic cancer research in China. Therefore, China needs to develop a multicenter cooperative research system for pancreatic cancer, take part in international multicenter clinical trials, or join an international cooperative group for pancreatic cancer.

CHALLENGES AND FUTURE DIRECTION

Each year more than 330000 patients are diagnosed with pancreatic cancer worldwide, with survival changing little in the last four decades. The incidence and mortality of pancreatic cancer in China are both increasing. According to the recent prediction from GLOBOCAN 2012, about 77497 men and 52868 women in China will be diagnosed with pancreatic cancer in 2035. Nearly 130000 patients will die from pancreatic cancer annually until then (Figure 10). The prediction means that the incidence and mortality of pancreatic cancer in China may increase faster in the next few years, and China will face a huge pancreatic cancer burden.

Unlike some cancers, pancreatic cancer is difficult

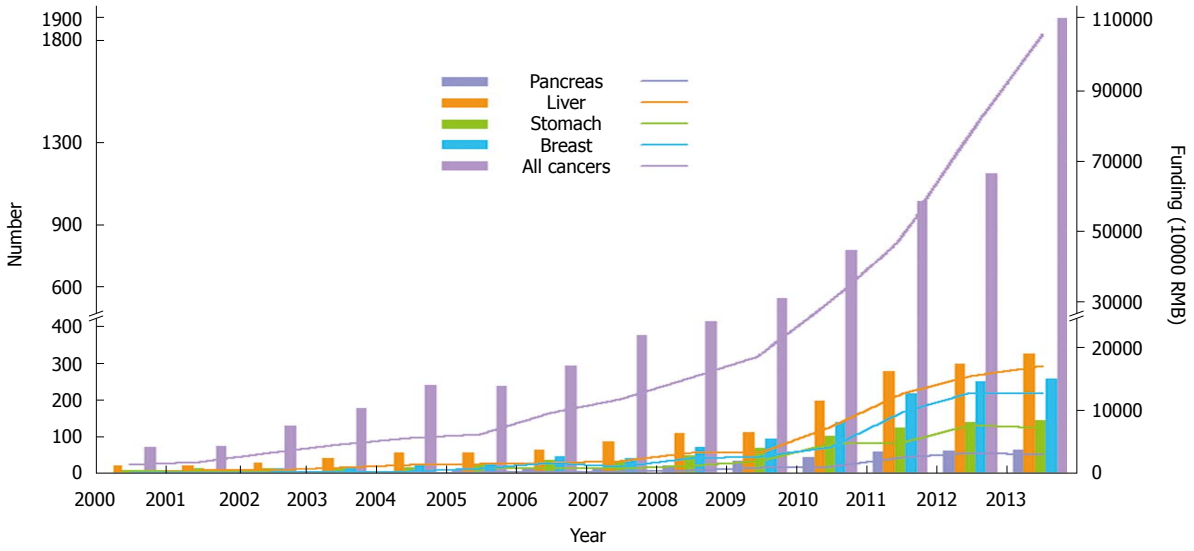

Figure 9 Numbers and research funding of National Natural Science Foundation of China about pancreatic cancer and other major malignancies over time.

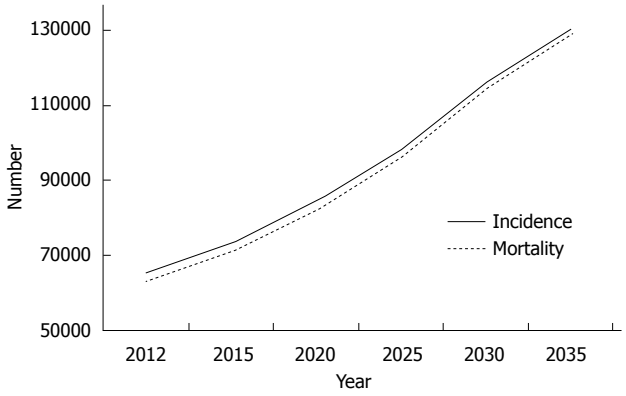

Figure 10 Estimated pancreatic cancer incidence and mortality in the next 20 years in China according to Globocan 2012.

to detect early, and usually presents at a late stage. With no established screening programs, resources might be allocated for earlier stage detection by offering a comprehensive strategy of imaging and genetics to identify curable cancers in high-risk individuals[111]. Some patients are overtreated with aggressive surgery or adjuvant therapy, while some are undertreated. Multidisciplinary care, which provides comprehensive evaluation and treatment, is the most effective approach to manage cancer patients[112]. However, multidisciplinary teams specialized in pancreatic cancer are currently rarely established in most centers in China, even in high-volume centers. Thus, multidisciplinary management of pancreatic cancer is an urgent need. Although more and more pancreatic cancer centers appear in China, rare multicenter collaborative studies have been conducted. The Chinese government should recognize shortfalls in research funding in areas of pancreatic cancer. More research supported by government funding can help us understand the biological behavior of pancreatic cancer and achieve successful treatment. Increased investment in education and healthcare are needed in order to upgrade the quality of care and to reduce the morbidity and mortality of pancreatic cancer. Last but not least, to improve national pancreatic cancer incidence and mortality statistics, the number of cancer registries still needs to be expanded, covering as much of the population as possible.

REFERENCES

1 **Ryan DP**, Hong TS, Bardeesy N. Pancreatic adenocarcinoma. *N Engl J Med* 2014; **371**: 1039-1049 [PMID: 25207767 DOI: 10.1056/NEJMra1404198]

2 **Zell JA**, Rhee JM, Ziogas A, Lipkin SM, Anton-Culver H. Race, socioeconomic status, treatment, and survival time among pancreatic cancer cases in California. *Cancer Epidemiol Biomarkers Prev* 2007; **16**: 546-552 [PMID: 17372250 DOI: 10.1158/1055-9965.EPI-06-0893]

3 **Lau MK**, Davila JA, Shaib YH. Incidence and survival of pancreatic head and body and tail cancers: a population-based study in the United States. *Pancreas* 2010; **39**: 458-462 [PMID: 19924019 DOI: 10.1097/MPA.0b013e3181bd6489]

4 **Quaresma M**, Coleman MP, Rachet B. 40-year trends in an index of survival for all cancers combined and survival adjusted for age and sex for each cancer in England and Wales, 1971-2011: a population-based study. *Lancet* 2015; **385**: 1206-1218 [PMID: 25479696 DOI: 10.1016/S0140-6736(14)61396-9]

5 **Ferlay J**, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. Lyon, France: International Agency for Research on Cancer, 2013. Available from: URL: http://globocan.iarc.fr, accessed on 18/1/2015

6 **Siegel RL**, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin* 2015; **65**: 5-29 [PMID: 25559415 DOI: 10.3322/caac.21254]

7 **Chen W**, Zheng R, Zhang S, Zhao P, Zeng H, Zou X. Report of cancer incidence and mortality in China, 2010. *Ann Transl Med* 2014; **2**: 61 [PMID: 25333036 DOI: 10.3978/j.issn.2305-5839.2014.04.05]

8 **Jemal A**, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA*

Cancer J Clin 2010; **60**: 277-300 [PMID: 20610543 DOI: 10.3322/caac.20073]
9 **Chen W**, Zheng R, Zhang S, Zhao P, Li G, Wu L, He J. Report of incidence and mortality in China cancer registries, 2009. *Chin J Cancer Res* 2013; **25**: 10-21 [PMID: 23372337 DOI: 10.3978/j.issn.1000-9604.2012.12.04]
10 **He J**, Chen WQ. Chinese Cancer Registry Annual Report 2012. Beijing: Press of Military Medical Sciences, 2012: 68-71
11 **Chen WQ**, Liang D, Zhang SW, Zheng RS, He YT. Pancreatic cancer incidence and mortality patterns in china, 2009. *Asian Pac J Cancer Prev* 2013; **14**: 7321-7324 [PMID: 24460295 DOI: 10.7314/APJCP.2013.14.12.7321]
12 **Pourhoseingholi MA**, Vahedi M, Baghestani AR. Burden of gastrointestinal cancer in Asia; an overview. *Gastroenterol Hepatol Bed Bench* 2015; **8**: 19-27 [PMID: 25584172]
13 **Baxter NN**, Whitson BA, Tuttle TM. Trends in the treatment and outcome of pancreatic cancer in the United States. *Ann Surg Oncol* 2007; **14**: 1320-1326 [PMID: 17225980 DOI: 10.1245/s10434-006-9249-8]
14 **Watts J**. China's environmental health challenges. *Lancet* 2008; **372**: 1451-1452 [PMID: 18975391]
15 **Kan H**. Environment and health in china: challenges and opportunities. *Environ Health Perspect* 2009; **117**: A530-A531 [PMID: 20049177 DOI: 10.1289/ehp.0901615]
16 **Jemal A**, Simard EP, Xu J, Ma J, Anderson RN. Selected cancers with increasing mortality rates by educational attainment in 26 states in the United States, 1993-2007. *Cancer Causes Control* 2013; **24**: 559-565 [PMID: 22729932 DOI: 10.1007/s10552-012-9993-y]
17 **Lynch SM**, Vrieling A, Lubin JH, Kraft P, Mendelsohn JB, Hartge P, Canzian F, Steplowski E, Arslan AA, Gross M, Helzlsouer K, Jacobs EJ, LaCroix A, Petersen G, Zheng W, Albanes D, Amundadottir L, Bingham SA, Boffetta P, Boutron-Ruault MC, Chanock SJ, Clipp S, Hoover RN, Jacobs K, Johnson KC, Kooperberg C, Luo J, Messina C, Palli D, Patel AV, Riboli E, Shu XO, Rodriguez Suarez L, Thomas G, Tjønneland A, Tobias GS, Tong E, Trichopoulos D, Virtamo J, Ye W, Yu K, Zeleniuch-Jacquette A, Bueno-de-Mesquita HB, Stolzenberg-Solomon RZ. Cigarette smoking and pancreatic cancer: a pooled analysis from the pancreatic cancer cohort consortium. *Am J Epidemiol* 2009; **170**: 403-413 [PMID: 19561064 DOI: 10.1093/aje/kwp134]
18 **Ferlay J**, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; **127**: 2893-2917 [PMID: 21351269 DOI: 10.1002/ijc.25516]
19 **Wang Y**, Duan H, Yang X, Guo J. Cigarette smoking and the risk of pancreatic cancer: a case-control study. *Med Oncol* 2014; **31**: 184 [PMID: 25159284 DOI: 10.1007/s12032-014-0184-4]
20 **Yin M**, Ma C, Liu S, Qian P, Zhang M, Chen W, Zheng R, Zhang S, Sun X. Cigarette Smoking and The Risk of Pancreatic Cancer: A Case -control Study. *Zhongguo Zhongliu* 2014; **3**: 200-204
21 **Vrieling A**, Bueno-de-Mesquita HB, Boshuizen HC, Michaud DS, Severinsen MT, Overvad K, Olsen A, Tjønneland A, Clavel-Chapelon F, Boutron-Ruault MC, Kaaks R, Rohrmann S, Boeing H, Nöthlings U, Trichopoulou A, Moutsiou E, Dilis V, Palli D, Krogh V, Panico S, Tumino R, Vineis P, van Gils CH, Peeters PH, Lund E, Gram IT, Rodríguez L, Agudo A, Larrañaga N, Sánchez MJ, Navarro C, Barricarte A, Manjer J, Lindkvist B, Sund M, Ye W, Bingham S, Khaw KT, Roddam A, Key T, Boffetta P, Duell EJ, Jenab M, Gallo V, Riboli E. Cigarette smoking, environmental tobacco smoke exposure and pancreatic cancer risk in the European Prospective Investigation into Cancer and Nutrition. *Int J Cancer* 2010; **126**: 2394-2403 [PMID: 19790196 DOI: 10.1002/ijc.24907]
22 **Chuang SC**, Gallo V, Michaud D, Overvad K, Tjønneland A, Clavel-Chapelon F, Romieu I, Straif K, Palli D, Pala V, Tumino R, Sacerdote C, Panico S, Peeters PH, Lund E, Gram IT, Manjer J, Borgquist S, Riboli E, Vineis P. Exposure to environmental tobacco smoke in childhood and incidence of cancer in adulthood in never smokers in the European Prospective Investigation into Cancer and Nutrition. *Cancer Causes Control* 2011; **22**: 487-494 [PMID: 21279734 DOI: 10.1007/s10552-010-9723-2]
23 **Wörmann SM**, Algül H. Risk factors and therapeutic targets in pancreatic cancer. *Front Oncol* 2013; **3**: 282 [PMID: 24303367 DOI: 10.3389/fonc.2013.00282]
24 **Li D**, Morris JS, Liu J, Hassan MM, Day RS, Bondy ML, Abbruzzese JL. Body mass index and risk, age of onset, and survival in patients with pancreatic cancer. *JAMA* 2009; **301**: 2553-2562 [PMID: 19549972 DOI: 10.1001/jama.2009.886]
25 **Larsson SC**, Orsini N, Wolk A. Body mass index and pancreatic cancer risk: A meta-analysis of prospective studies. *Int J Cancer* 2007; **120**: 1993-1998 [PMID: 17266034 DOI: 10.1002/ijc.22535]
26 **Bracci PM**. Obesity and pancreatic cancer: overview of epidemiologic evidence and biologic mechanisms. *Mol Carcinog* 2012; **51**: 53-63 [PMID: 22162231 DOI: 10.1002/mc.20778]
27 **Larsson SC**, Håkansson N, Giovannucci E, Wolk A. Folate intake and pancreatic cancer incidence: a prospective study of Swedish women and men. *J Natl Cancer Inst* 2006; **98**: 407-413 [PMID: 16537833 DOI: 10.1093/jnci/djj094]
28 **Jansen RJ**, Robinson DP, Stolzenberg-Solomon RZ, Bamlet WR, de Andrade M, Oberg AL, Rabe KG, Anderson KE, Olson JE, Sinha R, Petersen GM. Nutrients from fruit and vegetable consumption reduce the risk of pancreatic cancer. *J Gastrointest Cancer* 2013; **44**: 152-161 [PMID: 23620017 DOI: 10.1007/s12029-012-9441-y]
29 **Liu SZ**, Chen WQ, Wang N, Yin MM, Sun XB, He YT. Dietary factors and risk of pancreatic cancer: a multi-centre case-control study in China. *Asian Pac J Cancer Prev* 2014; **15**: 7947-7950 [PMID: 25292092 DOI: 10.7314/APJCP.2014.15.18.7947]
30 **Wang J**, Zhang W, Sun L, Yu H, Ni QX, Risch HA, Gao YT. Dietary energy density is positively associated with risk of pancreatic cancer in urban Shanghai Chinese. *J Nutr* 2013; **143**: 1626-1629 [PMID: 23902959 DOI: 10.3945/jn.113.178129]
31 **Soliman PT**, Cui X, Zhang Q, Hankinson SE, Lu KH. Circulating adiponectin levels and risk of endometrial cancer: the prospective Nurses' Health Study. *Am J Obstet Gynecol* 2011; **204**: 167.e1-167.e5 [PMID: 21047616 DOI: 10.1016/j.ajog.2010.08.045]
32 **Zhang J**, Dhakal IB, Gross MD, Lang NP, Kadlubar FF, Harnack LJ, Anderson KE. Physical activity, diet, and pancreatic cancer: a population-based, case-control study in Minnesota. *Nutr Cancer* 2009; **61**: 457-465 [PMID: 19838917 DOI: 10.1080/01635580902718941]
33 **Chari ST**, Leibson CL, Rabe KG, Timmons LJ, Ransom J, de Andrade M, Petersen GM. Pancreatic cancer-associated diabetes mellitus: prevalence and temporal association with diagnosis of cancer. *Gastroenterology* 2008; **134**: 95-101 [PMID: 18061176 DOI: 10.1053/j.gastro.2007.10.040]
34 **Pannala R**, Leirness JB, Bamlet WR, Basu A, Petersen GM, Chari ST. Prevalence and clinical profile of pancreatic cancer-associated diabetes mellitus. *Gastroenterology* 2008; **134**: 981-987 [PMID: 18395079 DOI: 10.1053/j.gastro.2008.01.039]
35 **Everhart J**, Wright D. Diabetes mellitus as a risk factor for pancreatic cancer. A meta-analysis. *JAMA* 1995; **273**: 1605-1609 [PMID: 7745774 DOI: 10.1001/jama.1995.03520440059037]
36 **Huxley R**, Ansary-Moghaddam A, Berrington de González A, Barzi F, Woodward M. Type-II diabetes and pancreatic cancer: a meta-analysis of 36 studies. *Br J Cancer* 2005; **92**: 2076-2083 [PMID: 15886696 DOI: 10.1038/sj.bjc.6602619]
37 **Ben Q**, Xu M, Ning X, Liu J, Hong S, Huang W, Zhang H, Li Z. Diabetes mellitus and risk of pancreatic cancer: A meta-analysis of cohort studies. *Eur J Cancer* 2011; **47**: 1928-1937 [PMID: 21458985 DOI: 10.1016/j.ejca.2011.03.003]
38 **Pannala R**, Basu A, Petersen GM, Chari ST. New-onset diabetes: a potential clue to the early diagnosis of pancreatic cancer. *Lancet Oncol* 2009; **10**: 88-95 [PMID: 19111249 DOI: 10.1016/S1470-2045(08)70337-1]
39 **Zhang PH**, Chen ZW, Lv D, Xu YY, Gu WL, Zhang XH, Le YL, Zhu HH, Zhu YM. Increased risk of cancer in patients with type 2 diabetes mellitus: a retrospective cohort study in China. *BMC Public Health* 2012; **12**: 567 [PMID: 22839452 DOI: 10.1186/1471-2458-12-567]

40 **Kuang TT**, Jin da Y, Wang DS, Xu XF, Ni XL, Wu WC, Lou WH. Clinical epidemiological analysis of the relationship between pancreatic cancer and diabetes mellitus: data from a single institution in China. *J Dig Dis* 2009; **10**: 26-29 [PMID: 19236544 DOI: 10.1111/j.1751-2980.2008.00359.x]

41 **Shi C**, Hruban RH, Klein AP. Familial pancreatic cancer. *Arch Pathol Lab Med* 2009; **133**: 365-374 [PMID: 19260742 DOI: 10.1043/1543-2165-133.3.365]

42 **Kastrinos F**, Stoffel EM. History, genetics, and strategies for cancer prevention in Lynch syndrome. *Clin Gastroenterol Hepatol* 2014; **12**: 715-727; quiz e41-3 [PMID: 23891921 DOI: 10.1016/j.cgh.2013.06.031]

43 **Bartsch DK**, Gress TM, Langer P. Familial pancreatic cancer--current knowledge. *Nat Rev Gastroenterol Hepatol* 2012; **9**: 445-453 [PMID: 22664588 DOI: 10.1038/nrgastro.2012.111]

44 **Raimondi S**, Lowenfels AB, Morselli-Labate AM, Maisonneuve P, Pezzilli R. Pancreatic cancer in chronic pancreatitis; aetiology, incidence, and early detection. *Best Pract Res Clin Gastroenterol* 2010; **24**: 349-358 [PMID: 20510834 DOI: 10.1016/j.bpg.2010.02.007]

45 **Lin G**, Zeng Z, Wang X, Wu Z, Wang J, Wang C, Sun Q, Chen Y, Quan H. Cholecystectomy and risk of pancreatic cancer: a meta-analysis of observational studies. *Cancer Causes Control* 2012; **23**: 59-67 [PMID: 22008981 DOI: 10.1007/s10552-011-9856-y]

46 **Gong Y**, Zhou Q, Zhou Y, Lin Q, Zeng B, Chen R, Li Z. Gastrectomy and risk of pancreatic cancer: systematic review and meta-analysis of observational studies. *Cancer Causes Control* 2012; **23**: 1279-1288 [PMID: 22674223 DOI: 10.1007/s10552-012-0005-z]

47 **Han-You X**. Chronic infection and other risk factors of cancer in China and other countries. *Ann Oncol* 2013; **24**: 267 [PMID: 23251013 DOI: 10.1093/annonc/mds598]

48 **Matthaei H**, Schulick RD, Hruban RH, Maitra A. Cystic precursors to invasive pancreatic cancer. *Nat Rev Gastroenterol Hepatol* 2011; **8**: 141-150 [PMID: 21383670 DOI: 10.1038/nrgastro.2011.2]

49 **Goss PE**, Strasser-Weippl K, Lee-Bychkovsky BL, Fan L, Li J, Chavarri-Guerra Y, Liedke PE, Pramesh CS, Badovinac-Crnjevic T, Sheikine Y, Chen Z, Qiao YL, Shao Z, Wu YL, Fan D, Chow LW, Wang J, Zhang Q, Yu S, Shen G, He J, Purushotham A, Sullivan R, Badwe R, Banavali SD, Nair R, Kumar L, Parikh P, Subramanian S, Chaturvedi P, Iyer S, Shastri SS, Digumarti R, Soto-Perez-de-Celis E, Adilbay D, Semiglazov V, Orlov S, Kaidarova D, Tsimafeyeu I, Tatishchev S, Danishevskiy KD, Hurlbert M, Vail C, St Louis J, Chan A. Challenges to effective cancer control in China, India, and Russia. *Lancet Oncol* 2014; **15**: 489-538 [PMID: 24731404 DOI: 10.1016/S1470-2045(14)70029-4]

50 **Ancona C**, Badaloni C, Mataloni F, Bolignano A, Bucci S, Cesaroni G, Sozzi R, Davoli M, Forastiere F. Mortality and morbidity in a population exposed to multiple sources of air pollution: A retrospective cohort study using air dispersion models. *Environ Res* 2015; **137**: 467-474 [PMID: 25701728 DOI: 10.1016/j.envres.2014.10.036]

51 **Campbell PJ**, Yachida S, Mudie LJ, Stephens PJ, Pleasance ED, Stebbings LA, Morsberger LA, Latimer C, McLaren S, Lin ML, McBride DJ, Varela I, Nik-Zainal SA, Leroy C, Jia M, Menzies A, Butler AP, Teague JW, Griffin CA, Burton J, Swerdlow H, Quail MA, Stratton MR, Iacobuzio-Donahue C, Futreal PA. The patterns and dynamics of genomic instability in metastatic pancreatic cancer. *Nature* 2010; **467**: 1109-1113 [PMID: 20981101 DOI: 10.1038/nature09460]

52 **Yachida S**, Jones S, Bozic I, Antal T, Leary R, Fu B, Kamiyama M, Hruban RH, Eshleman JR, Nowak MA, Velculescu VE, Kinzler KW, Vogelstein B, Iacobuzio-Donahue CA. Distant metastasis occurs late during the genetic evolution of pancreatic cancer. *Nature* 2010; **467**: 1114-1117 [PMID: 20981102 DOI: 10.1038/nature09515]

53 **Chu D**, Kohlmann W, Adler DG. Identification and screening of individuals at increased risk for pancreatic cancer with emphasis on known environmental and genetic factors and hereditary syndromes. *JOP* 2010; **11**: 203-212 [PMID: 20442513]

54 **Egawa S**, Takeda K, Fukuyama S, Motoi F, Sunamura M, Matsuno S. Clinicopathological aspects of small pancreatic cancer. *Pancreas* 2004; **28**: 235-240 [PMID: 15084963]

55 **Ariyama J**, Suyama M, Ogawa K, Ikari T. [Screening of pancreatic neoplasms and the diagnostic rate of small pancreatic neoplasms]. *Nihon Rinsho* 1986; **44**: 1729-1734 [PMID: 3537369]

56 **Zhao YP**. Pay attention to early diagnosis: the key to overcome pancreatic cancer. *Zhonghua Wai Ke Zazhi* 2001; **39**: 261-262

57 **Ni QX**, Yang F. Regulate diagnosis and treatment, increase the long-term survival rate of pancreatic cancer. *Zhongguo Puwai Jizhu Yu Linchuang Zazhi* 2006; **13**: 493-495

58 **Stoita A**, Penman ID, Williams DB. Review of screening for pancreatic cancer in high risk individuals. *World J Gastroenterol* 2011; **17**: 2365-2371 [PMID: 21633635 DOI: 10.3748/wjg.v17.i19.2365]

59 **Lee ES**, Lee JM. Imaging diagnosis of pancreatic cancer: a state-of-the-art review. *World J Gastroenterol* 2014; **20**: 7864-7877 [PMID: 24976723 DOI: 10.3748/wjg.v20.i24.7864]

60 **Poruk KE**, Firpo MA, Adler DG, Mulvihill SJ. Screening for pancreatic cancer: why, how, and who? *Ann Surg* 2013; **257**: 17-26 [PMID: 22895395 DOI: 10.1097/SLA.0b013e31825ffbfb]

61 **Canto MI**, Harinck F, Hruban RH, Offerhaus GJ, Poley JW, Kamel I, Nio Y, Schulick RS, Bassi C, Kluijt I, Levy MJ, Chak A, Fockens P, Goggins M, Bruno M. International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. *Gut* 2013; **62**: 339-347 [PMID: 23135763 DOI: 10.1136/gutjnl-2012-303108]

62 **Hanada K**, Okazaki A, Hirano N, Izumi Y, Teraoka Y, Ikemoto J, Kanemitsu K, Hino F, Fukuda T, Yonehara S. Diagnostic strategies for early pancreatic cancer. *J Gastroenterol* 2015; **50**: 147-154 [PMID: 25501287 DOI: 10.1007/s00535-014-1026-z]

63 **Long J**, Luo GP, Xiao ZW, Liu ZQ, Guo M, Liu L, Liu C, Xu J, Gao YT, Zheng Y, Wu C, Ni QX, Li M, Yu X. Cancer statistics: current diagnosis and treatment of pancreatic cancer in Shanghai, China. *Cancer Lett* 2014; **346**: 273-277 [PMID: 24462819 DOI: 10.1016/j.canlet.2014.01.004]

64 **Topazian M**, Enders F, Kimmey M, Brand R, Chak A, Clain J, Cunningham J, Eloubeidi M, Gerdes H, Gress F, Jagannath S, Kantsevoy S, LeBlanc JK, Levy M, Lightdale C, Romagnuolo J, Saltzman JR, Savides T, Wiersema M, Woodward T, Petersen G, Canto M. Interobserver agreement for EUS findings in familial pancreatic-cancer kindreds. *Gastrointest Endosc* 2007; **66**: 62-67 [PMID: 17382940 DOI: 10.1016/j.gie.2006.09.018]

65 **Zhao YP**. The present situation and the future of diagnosis and treatment of pancreatic cancer. *Zhonghua Waike Zazhi* 2014; **52**: 641-643

66 **Kaur S**, Baine MJ, Jain M, Sasson AR, Batra SK. Early diagnosis of pancreatic cancer: challenges and new developments. *Biomark Med* 2012; **6**: 597-612 [PMID: 23075238 DOI: 10.2217/bmm.12.69]

67 **Chen Y**, Hao J, Ma W, Tang Y, Gao C, Hao X. Improvement in treatment and outcome of pancreatic ductal adenocarcinoma in north China. *J Gastrointest Surg* 2011; **15**: 1026-1034 [PMID: 21484493 DOI: 10.1007/s11605-011-1493-y]

68 **Zhang QH**, Ni QX. [Clinical analysis of 2340 cases of pancreatic cancer]. *Zhonghua Yi Xue Zazhi* 2004; **84**: 214-218 [PMID: 15059537]

69 **Luo J**, Xiao L, Wu C, Zheng Y, Zhao N. The incidence and survival rate of population-based pancreatic cancer patients: Shanghai Cancer Registry 2004-2009. *PLoS One* 2013; **8**: e76052 [PMID: 24130758 DOI: 10.1371/journal.pone.0076052]

70 **Yu J**, Blackford AL, Dal Molin M, Wolfgang CL, Goggins M. Time to progression of pancreatic ductal adenocarcinoma from low-to-high tumour stages. *Gut* 2015; Epub ahead of print [PMID: 25636698 DOI: 10.1136/gutjnl-2014-308653]

71 **Bassi C**, Falconi M, Salvia R, Mascetta G, Molinari E, Pederzoli P. Management of complications after pancreaticoduodenectomy in a high volume centre: results on 150 consecutive patients. *Dig Surg* 2001; **18**: 453-457; discussion 458 [PMID: 11799295]

72 **Clarke CN**, Sussman JJ, Abbott DE, Ahmad SA. Factors affecting readmission after pancreaticoduodenectomy. *Adv Surg* 2013; **47**: 99-110 [PMID: 24298846]

73 **Lee GC**, Fong ZV, Ferrone CR, Thayer SP, Warshaw AL, Lillemoe KD, Fernández-del Castillo C. High performing whipple patients: factors associated with short length of stay after open pancreaticoduodenectomy. *J Gastrointest Surg* 2014; **18**: 1760-1769 [PMID: 25091843 DOI: 10.1007/s11605-014-2604-3]

74 **Brennan DD**, Zamboni GA, Raptopoulos VD, Kruskal JB. Comprehensive preoperative assessment of pancreatic adenocarcinoma with 64-section volumetric CT. *Radiographics* 2007; **27**: 1653-1666 [PMID: 18025509 DOI: 10.1148/rg.276075034]

75 **Yang F**, Jin C, Fu D. Celiac axis compression syndrome and pancreatic head cancer. *Pancreatology* 2014; **14**: 310-311 [PMID: 25207337]

76 **Gusmini S**, Nicoletti R, Martinenghi C, Del Maschio A. Vascular involvement in periampullary tumors: MDCT, EUS, and CDU. *Abdom Imaging* 2009; **34**: 514-522 [PMID: 18587612 DOI: 10.1007/s00261-008-9439-x]

77 **Sandrasegaran K**, Lin C, Akisik FM, Tann M. State-of-the-art pancreatic MRI. *AJR Am J Roentgenol* 2010; **195**: 42-53 [PMID: 20566796 DOI: 10.2214/AJR.10.4421]

78 **Dibble EH**, Karantanis D, Mercier G, Peller PJ, Kachnic LA, Subramaniam RM. PET/CT of cancer patients: part 1, pancreatic neoplasms. *AJR Am J Roentgenol* 2012; **199**: 952-967 [PMID: 23096166 DOI: 10.2214/AJR.11.8182]

79 **Wang XY**, Yang F, Jin C, Fu DL. Utility of PET/CT in diagnosis, staging, assessment of resectability and metabolic response of pancreatic cancer. *World J Gastroenterol* 2014; **20**: 15580-15589 [PMID: 25400441 DOI: 10.3748/wjg.v20.i42.15580]

80 **Rohren EM**, Turkington TG, Coleman RE. Clinical applications of PET in oncology. *Radiology* 2004; **231**: 305-332 [PMID: 15044750 DOI: 10.1148/radiol.2312021185]

81 **von Schulthess GK**, Steinert HC, Hany TF. Integrated PET/CT: current applications and future directions. *Radiology* 2006; **238**: 405-422 [PMID: 16436809 DOI: 10.1148/radiol.2382041977]

82 **Ngamruengphong S**, Swanson KM, Shah ND, Wallace MB. Preoperative endoscopic ultrasound-guided fine needle aspiration does not impair survival of patients with resected pancreatic cancer. *Gut* 2015; **64**: 1105-1110 [PMID: 25575893 DOI: 10.1136/gutjnl-2014-307475]

83 **Michalski CW**, Kleeff J, Wente MN, Diener MK, Büchler MW, Friess H. Systematic review and meta-analysis of standard and extended lymphadenectomy in pancreaticoduodenectomy for pancreatic cancer. *Br J Surg* 2007; **94**: 265-273 [PMID: 17318801]

84 **Yan JF**, Xu XW, Jin WW, Huang CJ, Chen K, Zhang RC, Harsha A, Mou YP. Laparoscopic spleen-preserving distal pancreatectomy for pancreatic neoplasms: a retrospective study. *World J Gastroenterol* 2014; **20**: 13966-13972 [PMID: 25320534 DOI: 10.3748/wjg.v20.i38.13966]

85 **Zhan Q**, Deng XX, Han B, Liu Q, Shen BY, Peng CH, Li HW. Robotic-assisted pancreatic resection: a report of 47 cases. *Int J Med Robot* 2013; **9**: 44-51 [PMID: 23225335 DOI: 10.1002/rcs.1475]

86 **Venkat R**, Edil BH, Schulick RD, Lidor AO, Makary MA, Wolfgang CL. Laparoscopic distal pancreatectomy is associated with significantly less overall morbidity compared to the open technique: a systematic review and meta-analysis. *Ann Surg* 2012; **255**: 1048-1059 [PMID: 22511003 DOI: 10.1097/SLA.0b013e318251ee09]

87 **Daouadi M**, Zureikat AH, Zenati MS, Choudry H, Tsung A, Bartlett DL, Hughes SJ, Lee KK, Moser AJ, Zeh HJ. Robot-assisted minimally invasive distal pancreatectomy is superior to the laparoscopic technique. *Ann Surg* 2013; **257**: 128-132 [PMID: 22868357 DOI: 10.1097/SLA.0b013e31825fff08]

88 **Croome KP**, Farnell MB, Que FG, Reid-Lombardo KM, Truty MJ, Nagorney DM, Kendrick ML. Total laparoscopic pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: oncologic advantages over open approaches? *Ann Surg* 2014; **260**: 633-638; discussion 638-640 [PMID: 25203880 DOI: 10.1097/SLA.0000000000000937]

89 **Jin C**, Yao L, Long J, Fu DL, Yu XJ, Xu J, Yang F, Ni QX. Effect of multiple-phase regional intra-arterial infusion chemotherapy on patients with resectable pancreatic head adenocarcinoma. *Chin Med J* (Engl) 2009; **122**: 284-290 [PMID: 19236805]

90 **Yang F**, Di Y, Li J, Wang XY, Yao L, Hao SJ, Jiang YJ, Jin C, Fu DL. Accuracy of routine multidetector computed tomography to identify arterial variants in patients scheduled for pancreaticoduodenectomy. *World J Gastroenterol* 2015; **21**: 969-976 [PMID: 25624732 DOI: 10.3748/wjg.v21.i3.969]

91 **Conroy T**, Desseigne F, Ychou M, Bouché O, Guimbaud R, Bécouarn Y, Adenis A, Raoul JL, Gourgou-Bourgade S, de la Fouchardière C, Bennouna J, Bachet JB, Khemissa-Akouz F, Péré-Vergé D, Delbaldo C, Assenat E, Chauffert B, Michel P, Montoto-Grillot C, Ducreux M. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med* 2011; **364**: 1817-1825 [PMID: 21561347 DOI: 10.1056/NEJMoa1011923]

92 **Von Hoff DD**, Ervin T, Arena FP, Chiorean EG, Infante J, Moore M, Seay T, Tjulandin SA, Ma WW, Saleh MN, Harris M, Reni M, Dowden S, Laheru D, Bahary N, Ramanathan RK, Tabernero J, Hidalgo M, Goldstein D, Van Cutsem E, Wei X, Iglesias J, Renschler MF. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med* 2013; **369**: 1691-1703 [PMID: 24131140 DOI: 10.1056/NEJMoa1304369]

93 **Ueno H**, Ioka T, Ikeda M, Ohkawa S, Yanagimoto H, Boku N, Fukutomi A, Sugimori K, Baba H, Yamao K, Shimamura T, Sho M, Kitano M, Cheng AL, Mizumoto K, Chen JS, Furuse J, Funakoshi A, Hatori T, Yamaguchi T, Egawa S, Sato A, Ohashi Y, Okusaka T, Tanaka M. Randomized phase III study of gemcitabine plus S-1, S-1 alone, or gemcitabine alone in patients with locally advanced and metastatic pancreatic cancer in Japan and Taiwan: GEST study. *J Clin Oncol* 2013; **31**: 1640-1648 [PMID: 23547081 DOI: 10.1200/JCO.2012.43.3680]

94 **Zhang DS**, Wang DS, Wang ZQ, Wang FH, Luo HY, Qiu MZ, Wang F, Li YH, Xu RH. Phase I/II study of albumin-bound nab-paclitaxel plus gemcitabine administered to Chinese patients with advanced pancreatic cancer. *Cancer Chemother Pharmacol* 2013; **71**: 1065-1072 [PMID: 23483298 DOI: 10.1007/s00280-013-2102-4]

95 **Ge F**, Xu N, Bai Y, Ba Y, Zhang Y, Li F, Xu H, Jia R, Wang Y, Lin L, Xu J. S-1 as monotherapy or in combination with leucovorin as second-line treatment in gemcitabine-refractory advanced pancreatic cancer: a randomized, open-label, multicenter, phase II study. *Oncologist* 2014; **19**: 1133-1134 [PMID: 25273077 DOI: 10.1634/theoncologist.2014-0223]

96 **Moore MJ**, Goldstein D, Hamm J, Figer A, Hecht JR, Gallinger S, Au HJ, Murawa P, Walde D, Wolff RA, Campos D, Lim R, Ding K, Clark G, Voskoglou-Nomikos T, Ptasynski M, Parulekar W. Erlotinib plus gemcitabine compared with gemcitabine alone in patients with advanced pancreatic cancer: a phase III trial of the National Cancer Institute of Canada Clinical Trials Group. *J Clin Oncol* 2007; **25**: 1960-1966 [PMID: 17452677]

97 **Guo XZ**, Cui ZM, Liu X. Current developments, problems and solutions in the non-surgical treatment of pancreatic cancer. *World J Gastrointest Oncol* 2013; **5**: 20-28 [PMID: 23556053 DOI: 10.4251/wjgo.v5.i2.20]

98 **Van Cutsem E**, Vervenne WL, Bennouna J, Humblet Y, Gill S, Van Laethem JL, Verslype C, Scheithauer W, Shang A, Cosaert J, Moore MJ. Phase III trial of bevacizumab in combination with gemcitabine and erlotinib in patients with metastatic pancreatic cancer. *J Clin Oncol* 2009; **27**: 2231-2237 [PMID: 19307500 DOI: 10.1200/JCO.2008.20.0238]

99 **Kindler HL**, Niedzwiecki D, Hollis D, Sutherland S, Schrag D, Hurwitz H, Innocenti F, Mulcahy MF, O'Reilly E, Wozniak TF, Picus J, Bhargava P, Mayer RJ, Schilsky RL, Goldberg RM. Gemcitabine plus bevacizumab compared with gemcitabine plus placebo in patients with advanced pancreatic cancer: phase III trial of the Cancer and Leukemia Group B (CALGB 80303). *J Clin Oncol* 2010; **28**: 3617-3622 [PMID: 20606091 DOI: 10.1200/JCO.2010.28.1386]

100 **Mellon EA**, Springett GM, Hoffe SE, Hodul P, Malafa MP, Meredith KL, Fulp WJ, Zhao X, Shridhar R. Adjuvant radiotherapy

and lymph node dissection in pancreatic cancer treated with surgery and chemotherapy. *Cancer* 2014; **120**: 1171-1177 [PMID: 24390779 DOI: 10.1002/cncr.28543]

101 **Chen Y**, Sun XJ, Jiang TH, Mao AW. Combined radiochemotherapy in patients with locally advanced pancreatic cancer: a meta-analysis. *World J Gastroenterol* 2013; **19**: 7461-7471 [PMID: 24259979 DOI: 10.3748/wjg.v19.i42.7461]

102 **Ke QH**, Zhou SQ, Yang JY, Du W, Liang G, Lei Y, Luo F. S-1 plus gemcitabine chemotherapy followed by concurrent radiotherapy and maintenance therapy with S-1 for unresectable pancreatic cancer. *World J Gastroenterol* 2014; **20**: 13987-13992 [PMID: 25320537 DOI: 10.3748/wjg.v20.i38.13987]

103 **Fan L**, Strasser-Weippl K, Li JJ, St Louis J, Finkelstein DM, Yu KD, Chen WQ, Shao ZM, Goss PE. Breast cancer in China. *Lancet Oncol* 2014; **15**: e279-e289 [PMID: 24872111 DOI: 10.1016/S1470-2045(13)70567-9]

104 **McQuade JL**, Meng Z, Chen Z, Wei Q, Zhang Y, Bei W, Palmer JL, Cohen L. Utilization of and Attitudes towards Traditional Chinese Medicine Therapies in a Chinese Cancer Hospital: A Survey of Patients and Physicians. *Evid Based Complement Alternat Med* 2012; **2012**: 504507 [PMID: 23093982 DOI: 10.1155/2012/504507]

105 **Meng Z**, Garrett CR, Shen Y, Liu L, Yang P, Huo Y, Zhao Q, Spelman AR, Ng CS, Chang DZ, Cohen L. Prospective randomised evaluation of traditional Chinese medicine combined with chemotherapy: a randomised phase II study of wild toad extract plus gemcitabine in patients with advanced pancreatic adenocarcinomas. *Br J Cancer* 2012; **107**: 411-416 [PMID: 22782343 DOI: 10.1038/bjc.2012.283]

106 **Asher GN**, Spelman K. Clinical utility of curcumin extract. *Altern Ther Health Med* 2013; **19**: 20-22 [PMID: 23594449]

107 **Dhillon N**, Aggarwal BB, Newman RA, Wolff RA, Kunnumakkara AB, Abbruzzese JL, Ng CS, Badmaev V, Kurzrock R. Phase II trial of curcumin in patients with advanced pancreatic cancer. *Clin Cancer Res* 2008; **14**: 4491-4499 [PMID: 18628464]

108 **Kanai M**, Yoshimura K, Asada M, Imaizumi A, Suzuki C, Matsumoto S, Nishimura T, Mori Y, Masui T, Kawaguchi Y, Yanagihara K, Yazumi S, Chiba T, Guha S, Aggarwal BB. A phase I/II study of gemcitabine-based chemotherapy plus curcumin for patients with gemcitabine-resistant pancreatic cancer. *Cancer Chemother Pharmacol* 2011; **68**: 157-164 [PMID: 20859741 DOI: 10.1007/s00280-010-1470-2]

109 **Yang F**, Jin C, Subedi S, Lee CL, Wang Q, Jiang Y, Li J, Di Y, Fu D. Emerging inorganic nanomaterials for pancreatic cancer diagnosis and treatment. *Cancer Treat Rev* 2012; **38**: 566-579 [PMID: 22655679 DOI: 10.1016/j.ctrv.2012.02.003]

110 **Yang F**, Jin C, Jiang Y, Li J, Di Y, Ni Q, Fu D. Liposome based delivery systems in pancreatic cancer treatment: from bench to bedside. *Cancer Treat Rev* 2011; **37**: 633-642 [PMID: 21330062 DOI: 10.1016/j.ctrv.2011.01.006]

111 **Verna EC**, Hwang C, Stevens PD, Rotterdam H, Stavropoulos SN, Sy CD, Prince MA, Chung WK, Fine RL, Chabot JA, Frucht H. Pancreatic cancer screening in a prospective cohort of high-risk patients: a comprehensive strategy of imaging and genetics. *Clin Cancer Res* 2010; **16**: 5028-5037 [PMID: 20876795 DOI: 10.1158/1078-0432.CCR-09-3209]

112 **Wolfgang CL**, Herman JM, Laheru DA, Klein AP, Erdek MA, Fishman EK, Hruban RH. Recent progress in pancreatic cancer. *CA Cancer J Clin* 2013; **63**: 318-348 [PMID: 23856911 DOI: 10.3322/caac.21190]

P- Reviewer: Scaggiante B, Yamagata M **S- Editor**: Qi Y
L- Editor: Kerr C **E- Editor**: Ma S

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com

ISSN 1007-9327