

# World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2011 September 27; 3(9): 131-141





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*World Journal of Gastrointestinal Surgery* (*World J Gastrointest Surg*, *WJGS*, online ISSN 1948-9366, DOI: 10.4240), is a monthly, open-access, peer-reviewed journal supported by an editorial board of 336 experts in gastrointestinal surgery from 35 countries.

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*World Journal of Gastrointestinal Surgery*

**LAUNCH DATE**  
November 30, 2009

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**PUBLICATION DATE**  
September 27, 2011

**ISSN**  
ISSN 1948-9366 (online)

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## Sentinel lymph node biopsy for gastric cancer: Where do we stand?

Mehmet Fatih Can, Gokhan Yagci, Sadettin Cetiner

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 Received: June 9, 2011 Revised: August 27, 2011  
 Accepted: September 12, 2011  
 Published online: September 27, 2011

### Abstract

Development of sentinel node navigation surgery (SNNS) and advances in minimally invasive surgical techniques have greatly shaped the modern day approach to gastric cancer surgery. An extensive body of knowledge now exists on this type of clinical application but is principally composed of single institute studies. Certain dye tracers, such as isosulfan blue or patent blue violet, have been widely utilized with a notable amount of success; however, indocyanine green is gaining popularity. The double tracer method, a synchronized use of dye and radio-isotope tracers, appears to be superior to any of the dyes alone. In the meantime, the concepts of infrared ray electronic endoscopy, fluorescence imaging, nanoparticles and near-infrared technology are emerging as particularly promising alternative techniques. Hematoxylin and eosin staining remains the main method for the detection of sentinel lymph node (SLN) metastases. Several specialized centers have begun to employ immunohistochemical staining for this type of clinical analysis but the equipment costs involving the associated ultra-rapid processing

systems is limiting its widespread application. Laparoscopic function-preserving resection of primary tumor from the stomach in conjunction with lymphatic basin dissection navigated by SLN identification represents the current paramount of SNNS for early gastric cancer. Patients with cT3 stage or higher still require standard D2 dissection.

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**Key words:** Sentinel lymph node biopsy; Gastric cancer; Laparoscopy; Lymph node dissection; Lymphatic metastasis; Staining and labeling

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Can MF, Yagci G, Cetiner S. Sentinel lymph node biopsy for gastric cancer: Where do we stand? *World J Gastrointest Surg* 2011; 3(9): 131-137 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v3/i9/131.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v3.i9.131>

### INTRODUCTION

Over the past two decades, sentinel lymph node (SLN) biopsy in surgical oncology has been so successful that it is now considered as the gold standard procedure in breast cancer surgery. There is also a growing body of published research supporting the utility of SLN biopsy for gastrointestinal cancers, particularly with colorectal and gastric adenocarcinomas<sup>[1,2]</sup>. Compared to colorectal cancer surgery, however, investigations into SN biopsy for gastric malignancies are not as prevalent as those involving colorectal surgery. Concurrent advances in

laparoscopic techniques have stimulated many gastrointestinal surgeons to seek out new ways to easily perform SLN biopsy and to make more precise decisions as to the extent of lymphatic tissue that should be removed during laparoscopic resection of gastric cancer.

As one of the commonest cancers and the second most frequent cause of cancer-related deaths worldwide, carcinoma of the stomach affects hundreds of thousands of people every year<sup>[3]</sup>. Two of the most important prognostic factors for patients with gastric cancer are tumor depth and lymph node involvement. While complete resection of any gastric primary tumor can be sufficiently ensured by frozen section examination of the resected margins, the most effective means by which to manage the associated lymph nodes and lymphatic channels draining the tumoral area remain undefined. This clinical inconsistency stems from the fact that a given proportion of patients who present no lymph node metastasis undergo routine D2 lymphadenectomy as a standard procedure<sup>[4]</sup>. The emergence of new technologies, however, have facilitated the use of SN biopsy as a sufficiently reliable guide towards defining the boundaries of tissues to be resected during oncological surgery; this concept is now generally referred to as “sentinel node navigation surgery (SNNS)”<sup>[4]</sup>.

## GENERAL PERSPECTIVE OF THE STUDIES ON SNNS FOR TREATMENT OF GASTRIC CANCER

The principal objective of using sentinel node biopsy and SLN mapping is to limit the extent of tissue dissection around the primary organ. Ultimately, the SNL is expected to facilitate precise and sufficient resection while decreasing the risk of morbidity caused by unnecessary removal of tumor-free areas. Studies on the clinical use of SNNS for gastric cancers first appeared in the English literature in the early 2000s and have since led many oncological researchers and clinicians to develop new methods by which to improve the feasibility and usefulness of sentinel node mapping. In fact, over 50 studies to date have investigated SNNS for its specific applicability to treat gastric cancer. The majority of these studies have been published in journals indexed in the Medline® database<sup>[5-55]</sup> (Table 1). Not surprisingly, most of the studies in this field have been conducted in Japan, where adenocarcinoma of the stomach is considered endemic and remains the leading cause of cancer-related deaths<sup>[56]</sup>. Authors from South Korea are the second most prevalent publishers on this topic. Researchers interested in evaluating the effectiveness of SNNS for treating gastric cancer are usually practicing clinicians, probably since those tracers and methods commonly used in any form of SNNS were previously established by experimental studies in breast and colon cancer models. As a result, only one-tenth of the gastric cancer-related contributions have had a laboratory-based design<sup>[38,40,42,49,55]</sup>. Consider-

**Table 1 Relevant publications reporting on sentinel node concept for gastric cancer**

Author	Yr	Country	Study design	n
Hiratsuka <i>et al</i> <sup>[5]</sup>	2001	Japan	Clinical	74
Kitagawa <i>et al</i> <sup>[6]</sup>	2002	Japan	Clinical	145
Hundley <i>et al</i> <sup>[7]</sup>	2002	USA	Clinical	14
Ichikura <i>et al</i> <sup>[8]</sup>	2002	Japan	Clinical	62
Hayashi <i>et al</i> <sup>[9]</sup>	2003	Japan	Clinical	31
Ajisaka <i>et al</i> <sup>[10]</sup>	2003	Japan	Clinical	35
Miwa <i>et al</i> <sup>[11]</sup>	2003	Japan	Clinical	211
Ishigami <i>et al</i> <sup>[12]</sup>	2003	Japan	Clinical	27
Uenosono <i>et al</i> <sup>[13]</sup>	2003	Japan	Clinical	?
Ryu <i>et al</i> <sup>[14]</sup>	2003	South Korea	Clinical	71
Tonouchi <i>et al</i> <sup>[15]</sup>	2003	Japan	Clinical	17
Isozaki <i>et al</i> <sup>[16]</sup>	2004	Japan	Clinical	144
Nimura <i>et al</i> <sup>[17]</sup>	2004	Japan	Clinical	84
Kim <i>et al</i> <sup>[18]</sup>	2004	South Korea	Clinical	46
Tanaka <i>et al</i> <sup>[19]</sup>	2004	Japan	Clinical	3
Yasuda <i>et al</i> <sup>[20]</sup>	2004	Japan	Clinical	18
Osaka <i>et al</i> <sup>[21]</sup>	2004	Japan	Clinical	57
Tonouchi <i>et al</i> <sup>[22]</sup>	2005	Japan	Clinical	37
Lee <i>et al</i> <sup>[23]</sup>	2005	South Korea	Clinical	121
Gretschel <i>et al</i> <sup>[24]</sup>	2005	Germany	Clinical	34
Uenosono <i>et al</i> <sup>[25]</sup>	2005	Japan	Clinical	104
Zulfikaroglu <i>et al</i> <sup>[26]</sup>	2005	Turkey	Clinical	32
Arigami <i>et al</i> <sup>[27]</sup>	2006	Japan	Clinical	61
Ichikura <i>et al</i> <sup>[28]</sup>	2006	Japan	Clinical	80
Ishizaki <i>et al</i> <sup>[29]</sup>	2006	Japan	Clinical	101
Park <i>et al</i> <sup>[30]</sup>	2006	South Korea	Clinical	100
Lee <i>et al</i> <sup>[31]</sup>	2006	South Korea	Clinical	64
Mura <i>et al</i> <sup>[32]</sup>	2006	Italy	Clinical	10
Saikawa <i>et al</i> <sup>[33]</sup>	2006	Japan	Clinical	35
Ohdaira <i>et al</i> <sup>[34]</sup>	2007	Japan	Clinical	161
Morita <i>et al</i> <sup>[35]</sup>	2007	Japan	Clinical	53
Ishigami <i>et al</i> <sup>[36]</sup>	2007	Japan	Clinical	5
Rino <i>et al</i> <sup>[37]</sup>	2007	Japan	Clinical	43
Kitayama <i>et al</i> <sup>[38]</sup>	2007	Japan	Experimental	-
Gretschel <i>et al</i> <sup>[39]</sup>	2007	Germany	Clinical	35
Koyama <i>et al</i> <sup>[40]</sup>	2007	Japan	Experimental	-
Ishikawa <i>et al</i> <sup>[41]</sup>	2007	Japan	Clinical	16
Koyama <i>et al</i> <sup>[42]</sup>	2007	Japan	Experimental	-
Yaguchi <i>et al</i> <sup>[43]</sup>	2008	Japan	Clinical	63
Miyashiro <i>et al</i> <sup>[44]</sup>	2008	Japan	Clinical	3
Orsenigo <i>et al</i> <sup>[45]</sup>	2008	Italy	Clinical	34
Lee <i>et al</i> <sup>[46]</sup>	2008	Korea	Clinical	21
Yanagita <i>et al</i> <sup>[47]</sup>	2008	Japan	Clinical	133
Tajima <i>et al</i> <sup>[48]</sup>	2009	Japan	Clinical	56
Cahill <i>et al</i> <sup>[49]</sup>	2009	France	Experimental	-
Ichikura <i>et al</i> <sup>[50]</sup>	2009	Japan	Clinical	35
Ohdaira <i>et al</i> <sup>[51]</sup>	2009	Japan	Clinical	30
Park do <i>et al</i> <sup>[52]</sup>	2011	Korea	Clinical	68
Rabin <i>et al</i> <sup>[53]</sup>	2010	Israel	Clinical	80
Kelder <i>et al</i> <sup>[54]</sup>	2010	Japan	Clinical	212
Jeong <i>et al</i> <sup>[55]</sup>	2010	Korea	Experimental	-

ing knowledge accessible through the Medline® database, we can say that the total number of patients enrolled in studies evaluating SNNS feasibility for gastric cancer treatment - irrespective of the method used for the removal of primary tumor - stands at approximately 2800 (Table 1). In order to determine the potential of SNNS to detect lymph node involvement and identify the most accurate SNNS strategies, studies have examined a wide array of technical aspects, including but not limited to, the effectiveness of novel tracers, different injection sites



and methods and type of surgery performed. These efforts have yielded a rapid advancement in SNNS-based procedures compatible with newly developed technologies and have improved the ability of physicians to readily and precisely detect metastatic sentinel LNs. Today's questions regarding the usefulness of SNNS for treating gastric cancer may, therefore, be categorized into three groups: (1) What tracer should be used, and by which means, to identify SLNs? (2) What method should be selected for the detection of SLN metastasis? and (3) Which patient is suitable for SNNS and what strategy should be used to manage tumor load?

## WHAT TRACER SHOULD BE USED, AND BY WHICH MEANS, TO IDENTIFY SLNs?

An acceptable rate of success for detecting metastasis in SLN for gastric cancer can only be achieved by accurately identifying real sentinel nodes in a timely manner during the operation. Any ideal tracer for SNNS in gastric cancer would be characterized as a nontoxic, readily available and cost-effective substance that is capable of accumulating in the SLN within a few minutes, stays there for hours and does not escape beyond the sentinel nodes. This ideal tracer would also be expected to be conducive to use during both open and minimally invasive surgical techniques and easily recognizable by the surgeon without use of sophisticated equipment. To date, an ideal tracer that meets all of the above mentioned criteria has yet to be developed. In early studies of SNNS for use in gastric cancer surgery, dye-guided and radioisotope-guided methods represented the procedures of choice<sup>[5-12,14-16]</sup>. The dye agents most often used are isosulfan blue, patent blue violet and indocyanine green (ICG), while Technetium 99m-radiolabeled tin Colloid is the most frequently used radioisotope. Introduction of infrared ray electronic endoscopy (IREE)<sup>[17,34,41]</sup> followed these techniques to facilitate visualization of dyed SLNs and lymphatic basins draining the tumor as they are contrasted from the fatty areas surrounding the stomach. More recently, it has been suggested that fluorescence imaging of the lymphatic structures stained by ICG can be used to visualize the dye within thin lymphatic vessels and those SLNs situated deep within the tissue that might otherwise have been overlooked<sup>[44,48]</sup>. The most recent investigations into the development of precise detection methods for SLNs in gastric cancer are quite promising. For example, near-infrared fluorescence (NIR) technology combined with the use of quantum dots, a well-known nanoparticles group, as the tracer has been used successfully in pigs, allowing the surgeon to see both natural anatomical structures and SLNs in real time<sup>[57,58]</sup>. Furthermore, quantum dots rapidly map lymphatic vessels, accumulate into the SLNs within 1 to 3 min and do not flow toward non-sentinel nodes at any time over a 4 h period<sup>[58]</sup>. ATX-S10Na(II), a novel lysosomal photosensitizer, has been characterized for its ability to sustain the original injected concentration

for an extended period of time and can be visually identified by its bright red coloration in the lymphatic tissue; this chemical has been investigated in animal studies for its potential as a valid tracer<sup>[36,38,40,42]</sup>. Research continues to determine the properties of toxicity of these next generation tracers and it seems likely that in the near future these novel tracers will advance to replace conventional dye-guided and radioisotope-based methods in SNNS.

The issue of how to best administer any tracer has been another topic of debate. Traditional application mandates preoperative submucosal administration of radio-isotopes or intraoperative submucosal injection of dye tracer around the primary tumor, depending on the mapping method preferred by the physician. Both of these methods are carried out *via* endoscopy. A few studies have performed direct comparisons of submucosal vs subserosal injection of dye to determine which method yielded superior SLN detection rates. In a study of 121 patients, Lee *et al.*<sup>[23]</sup> compared the subserosal and submucosal injection of isosulfan blue. They found no significant difference between the two methods in terms of the proportion of successfully identified SLNs (92 and 94 percent, respectively) or the number of SLNs determined per patient (2.5 and 2.9, respectively). Likewise, Yaguchi *et al.*<sup>[43]</sup> determined that submucosal application by intraoperative endoscopy had similar rates of node identification as the subserosal injection of ICG introduced by physicians relying only on naked vision. Still, many other reports have presented data in favor of the endoscopic approach and most surgeons prefer endoscopy-assisted submucosal administration.

An overview of all the relevant studies on this topic on Medline demonstrated that two major trends have emerged in SNNS over the past 5 years. Firstly, a general preference for the double-tracer (dye plus isotope) method to visualize SLNs has arisen<sup>[31-33,35,39,43,46,52]</sup>. A number of authors have reported significant increases in the rate of successful identification of SLNs by combined use of both techniques<sup>[31-33,46,52,59]</sup>, although some studies have presented evidence that does not support this idea<sup>[39]</sup>. Hayashi *et al.*<sup>[9]</sup> concluded that use of only a single dye-guided or radio-guided method resulted in a reduced success rate; specifically, each method achieved only 90% of success in identifying SLNs and 4%-7% of skip metastasis to the non-SLNs. The second trend witnessed over the last 5 years is a remarkable increase in the use of ICG as the dye tracer for SNSS, as compared to the previously preferred isosulfan blue and patent blue violet dyes<sup>[28,30,34,35,48,51,54]</sup>. It is a fact that globalization has allowed increased availability to next generation tools and research materials to more countries and has enabled researchers to explore novel techniques within their own clinics.

In summary, although there still is no clear consensus as to the nature of tracer or superior method to accurately identify SNLs by SNNS in gastric cancer, some conclusions may be drawn. Firstly, the dual-mapping procedure continues to increase in popularity. Secondly,

endoscopic administration of the tracers (radio-isotope: 3 h to 1 d before surgery; dye: intraoperative) remains the procedure of choice. Thirdly, ICG with fluorescent imaging is rapidly gaining proponents. It should be recognized that the procedure selected will be dependent upon the capabilities of the surgeon and the medical facility where the health service is offered. This reality is a particular limiting factor for laparoscopic SNNS, which requires technical expertise and costly equipment. Most importantly, recent reports of novel products, such as quantum dots, and techniques, such as IREE and NIR, are highly promising for the future of SNNS.

## WHAT METHOD SHOULD BE SELECTED FOR THE DETECTION OF SLN METASTASIS?

An intraoperatively detected metastasis of an SLN during SNNS is the key factor that will determine whether a patient will proceed with conventional D2 lymph node dissection or not. As such, it is our opinion that the false negative and accuracy rate are of the utmost importance in SNNS for gastric cancer. Unfortunately, the outcomes of not performing a standard extended lymph node dissection on patients who were clear on SLN biopsy but actually had lymph node metastasis include increased rate of omitting adjuvant therapy and mortality rates.

The traditional practice of SLN for gastric carcinoma biopsy has been largely based on the use of hematoxylin and eosin (HE) staining for histological examination of frozen section slices. However, the issue of whether HE is adequate for intraoperative detection of LN metastasis remains controversial. Kitagawa *et al.*<sup>[59]</sup> reported that accurate intraoperative diagnosis using HE with a single slice was possible in only 74% of cases. Contrary to that conclusion, other authors have reported satisfactory accuracy rates (between 93.8% and 100%) with HE staining of SLN biopsied tissue<sup>[5,9,23,30,33,41,50]</sup>. Because of this controversy, efforts have been directed towards identifying more reliable histopathological methods. What we find interesting is that most of the studies that compared the conventional HE method with more sophisticated methods, such as immunohistochemical staining (IHC) and reverse transcription-polymerase chain reaction (RT-PCR), reported a significant improvement in the detection rate where the presence/absence of metastasis was confirmed using a sophisticated method. For example, in the study by Arigami *et al.*<sup>[27]</sup> that included 61 patients with cT1 and cT2 cN0 disease, HE was used to determine that five (8.2%) of the patients had SLN metastasis, whereas eight (13.1%) were found to have metastatic disease by the IHC method. This rate rose to 36.1% (22 patients) when RT-PCR was used for the diagnosis of metastasis. The difference in findings from the IHC and RT-PCR methods were due to micrometastases being demonstrated in 14 additional patients by the sensitive PCR-based technique. As the significance of micrometastases

for gastric carcinomas is still undefined, the presence of micrometastases, especially in early gastric cancer with no clinically evident lymph node metastasis, should be interpreted thoughtfully and rationally. Similarly, Osaka and colleagues showed that IHC and RT-PCR were able to detect micrometastases in 8 and 21 LNs, respectively, from 10 out of 57 patients with confirmed early gastric cancer<sup>[21]</sup>. None of those metastases were identifiable by conventional tissue staining. The results of the two latter studies suggest that the conventional HE method may not be sufficient to manage patients with early gastric cancer *via* the SLN concept. Unfortunately, methods relying on the amplification of certain mRNAs associated with malignant cells or staining by given monoclonal antibodies that react with a broad spectrum of human cytokeratins have two major drawbacks: firstly, the technical equipment is unavailable in many hospitals across the globe; and secondly, obtaining a timely result during surgery is difficult. It is clear that the rationality of a technique for SNNS is correlated with its applicability to intraoperative decision-making. Despite the time requirement being only 30-40 min to obtain an IHC result, only a limited number of centers around the world have the equipment and trained staff necessary to carry out such a test.

To summarize, it is necessary to note that the method selected to detect any metastasis in SLNs for gastric cancer is as important as the method used to identify those SLNs. However, for routine clinical care, HE with multiple slices seems the best available option that enables surgeons to make an intraoperative decision, despite its high risk of overlooking some micrometastases. If possible, supplementing the HE procedure with ultra-rapid IHC will definitely contribute to the reliability of the results. The RT-PCR method has yet to be established as a standard practice, mainly due to cost restrictions. Another solution may be that the entire lymphatic basin corresponding to the stained and/or radio-labeled SLNs is removed, regardless of the presence or absence of metastasis in SLNs.

## WHICH PATIENT IS SUITABLE FOR SNNS AND WHAT STRATEGY SHOULD BE USED TO MANAGE TUMOR LOAD?

Unlike breast cancer, carcinoma of the stomach has the distinctive property of loco-regional invasion. Multidirectional, rather than single-course, flow of lymphatic fluid from the primary tumor allows metastatic cells to move to multiple SLNs. This flow can be directed toward any number of SLNs situated anywhere throughout the lesser curvature (LNs No. 1, 3 and 5) (according to classification by the Japanese Gastric Cancer Association<sup>[3]</sup>) or the greater curvature (LNs No. 2, 4 and 6) in a manner that is generally relevant to the location of the primary lesion. However, this is not always the case. Multiple SLNs can also be present along both the lesser and greater curva-

tures concurrently<sup>[54]</sup>. Another probability is that some SLNs can be situated at the second echelon (LNs No. 7, 8, 9 and 11)<sup>[7,59]</sup>. This complicated drainage structure has been one of the most challenging obstacles that has restricted the efficacy of SNNS in patients with gastric cancer.

Perusal of the relevant literature reveals a truth unquestionable at this moment: it is possible to undertake SNNS but only for a certain subset of patients with gastric cancer, with proportions ranging from approximately as low as 3% to as high as 50%, depending on the country where the procedure is performed<sup>[1,53,56,60]</sup>. Studies from Japan and Korea have selectively included clinically node-negative cT1 and cT2 patients<sup>[6,9,10,17,18,21,23,43,52,54]</sup>, while studies originating from countries in the western regions have included cases with cT3 (serosal infiltration) tumors as well<sup>[7,24,26,53]</sup>. However, skip metastasis in gastric cancer has been associated with lymphatic obstruction by tumor cells that usually is accompanied by aberrant lymphatic pathways; this event makes the consideration of SNNS of cT3 tumors having a higher risk of LN involvement controversial<sup>[45,46,53]</sup>. Moreover, some authors have asserted that cT1, rather than cT2, tumors represented the best candidates for SNNS<sup>[30,48,52,59]</sup>. Fortunately, in many cases the skip metastasis is encountered in non-SLNs at the same lymphatic basin as the SLN. Therefore, removal of entire relevant lymphatic basin, rather than selective excision of identified SLNs, appears to be the most reliable procedure<sup>[11,46,52,59]</sup>.

As SNNS for gastric cancer aims to protect the patient from unnecessary morbidity by means of a less invasive dissection, the optimal procedure would integrate the use of laparoscopic or other minimally invasive approaches. Studies investigating SNNS for gastric cancer during open surgery first appeared in the literature in the early 2000s<sup>[5-11,18,21,24]</sup>. Over the last 5 years, data has been presented from use of the technique in amalgamated subsets of open and laparoscopic treatment<sup>[17,54]</sup> and in patients undergoing laparoscopic resection<sup>[22,45,46,48,52]</sup>. Interestingly, in a recent report based on an experimental study, Cahill *et al.*<sup>[49]</sup> claimed that SNNS could also be performed during natural orifice transluminal endoscopic surgery. Meanwhile, the laparoscopic approach is rapidly evolving into a key strategy in the armamentarium of gastric cancer surgery, owing to novel facilitating devices which may be used for both radical and partial resection of the stomach. The current knowledge supports the practice of laparoscopic lymphatic basin dissection plus function-preserving (partial or wedge) resection of the primary tumor, providing that it is smaller than 4 cm in diameter. The issue of whether patients with a primary lesion confined to the mucosa might also be viable candidates for endoscopic mucosal resection with SLN biopsy is under investigation and preliminary trials are reporting encouraging outcomes<sup>[61,62]</sup>. It seems feasible to perform distal, proximal or total gastrectomy, depending upon the lesion location, for those patients with more extensive lesions. Given promising instrumental revolutions and the

growing body of knowledge, it is logical to predict that the laparoscopic approach will soon become the standard of care for patients with clinically diagnosed node-negative early gastric cancer as it is complementary to the SNNS concept.

In conclusion, recent advances in SNNS and minimally invasive interventions have significantly impacted our current approaches to gastric cancer surgery. A number of reports representing single institute experiences have augmented the relevant knowledge base. The currently established double tracer method (dye and radio-isotope tracers) appears to be the most efficacious and reliable procedure for identifying true sentinel nodes. While conventional dye tracers, such as isosulfan blue or patent blue violet, are still useful, ICG deserves more attention for the current applications. IREE, fluorescence imaging, nanoparticles and near-infrared technology represent the future direction in which the SNNS concept is advancing. Across the globe, detection of SLNs harboring metastasis is mainly accomplished by HE staining. Immunohistochemical staining has considerable potential for routine clinical use; however, ultra-rapid processing systems must first become more prevalent among each country's hospitals. Laparoscopic function-preserving resection of the tumor from the stomach with lymphatic basin dissection navigated by SLN identification represents the current dominant choice of SNNS for early gastric cancer. Patients with cT3 or more advanced disease are still advised to receive standard D2 dissection for yielding satisfactory survival rates.

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



## Spleen preserving distal pancreatectomy in an isolated blunt pancreatic trauma

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Received: November 24, 2010 Revised: July 26, 2011

Accepted: August 5, 2011

Published online: September 27, 2011

atectomy; Spleen preservation; Blunt abdominal trauma; Splenectomy

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### Abstract

Blunt isolated pancreatic trauma is uncommon, accounting for 1%-4% of high impact abdominal injuries. In addition, its diagnosis can be difficult; physical signs may be poor and laboratory findings nonspecific, resulting in delayed treatment. Preserving the spleen during distal pancreatectomy (DP) is controversial. One of the spleen's functions regards immunity; complications following splenectomy include leukocytosis, thrombocytosis, overwhelming post splenectomy sepsis and some degree of immunodeficiency. This is why many authors favor its preservation. We describe a case of a young man with an isolated pancreatic trauma due to a blunt abdominal trauma with a delayed presentation who was treated with spleen-preserving DP and we discuss the value of this procedure with reference to the literature.

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**Key words:** Isolated pancreatic trauma; Distal pancre-

### INTRODUCTION

Blunt isolated pancreatic trauma is uncommon<sup>[1]</sup>, accounting for 1%-4% of high impact blunt abdominal injuries<sup>[2]</sup>. In addition, its diagnosis can be difficult; physical signs may be poor and laboratory findings nonspecific<sup>[1]</sup>, resulting in delayed treatment<sup>[3]</sup>. In many instances, the injury only becomes apparent after the development of complications<sup>[4]</sup>. Due to this, the management of these kinds of injuries is not easy and few surgeons and institutes have the necessary experience<sup>[1]</sup>.

Several treatment modalities have been described, from non-surgical to open drainage and even duodeno-pancreatectomy<sup>[3]</sup>, depending on the grade of the lesion. Major duct injury is the most important factor related to the outcome in these patients<sup>[3]</sup>. When present (incidence near to 1.3%), pancreaticojejunostomy and distal pancreatectomy (DP), with or without splenectomy, can be performed, the latter being preferred<sup>[3]</sup>.

Preserving the spleen during DP is controversial. Some authors found no significant difference with or without splenectomy<sup>[5]</sup>; the majority believe that the main-

tenance of the organ brings more benefits to the patient, as shown in their reports<sup>[6-12]</sup>. One of the spleen's functions is immunity; complications following splenectomy include leukocytosis, thrombocytosis, overwhelming post splenectomy sepsis and some degree of immunodeficiency<sup>[9]</sup>. These are the most common arguments made by authors favoring spleen preservation.

The spleen can be preserved in two different ways while performing a DP. Firstly, the splenic vessels are maintained, assuring adequate blood supply to the organ. Secondly, these vessels are ligated, preserving the short gastric vessels for perfusion. In the latter technique, macroscopic inspection of the spleen has been shown to be efficient and reliable<sup>[7,11]</sup>.

We describe the case of a young man with an isolated pancreatic trauma due to a blunt abdominal trauma with a delayed presentation who was treated with spleen-preserving DP and we discuss the value of this procedure with reference to the literature.

## CASE REPORT

LHGJ, 18 years old, male, had a motorcycle accident 24 h earlier and presented with a blunt abdominal trauma. He decided to get medical attention due to abdominal pain and vomiting. He was hemodynamically stable (arterial pressure: 120 × 80 mmHg and heart rate: 110 bpm). On physical examination, abdominal palpation was painful with no signs of peritonitis. Laboratory tests and a computed tomography (CT) of the abdomen were carried out. Results: amylase: 1237 U/L; creatinine: 1.7mg/dL; glucose: 125 mg/dL; hemoglobin: 15.6. Abdominal CT: fluid in the upper abdomen, with a pancreatic trauma with transection of the main pancreatic duct. Other organs showed no signs of injuries (Figure 1A and B). Due to the high suspicion of main pancreatic injury, a laparotomy was performed. At surgery, the fracture with duct disruption was confirmed (Figure 2); a spleen-preserving DP maintaining the splenic vessels was performed. We carried out specific ligation of the main pancreatic duct and a hand sewn interrupted suture of the pancreatic stump (Figure 3). The patient recovered uneventfully and was discharged on postoperative day 5.

## DISCUSSION

Trauma to the pancreas is a rare entity, especially when it is the only organ to be injured in an abdominal trauma<sup>[1,3,8,13]</sup>. This occurs due to its retroperitoneal location<sup>[3]</sup>. When it happens, physical examination can be poor and laboratory findings nonspecific<sup>[1]</sup>, leading to delayed diagnosis and treatment. Thus, this injury has high rates of morbidity and mortality, with overall complications rates up to 62%<sup>[1,3]</sup>, reaching 80% when diagnosis is made 24 h after injury<sup>[3]</sup>. The principal determinant of outcome in these patients is major duct involvement<sup>[1,3,14]</sup>. With the information above, one can understand why it is important to maintain a high suspicion in patients with unexplained abdominal signs after blunt trauma. Accurate and early

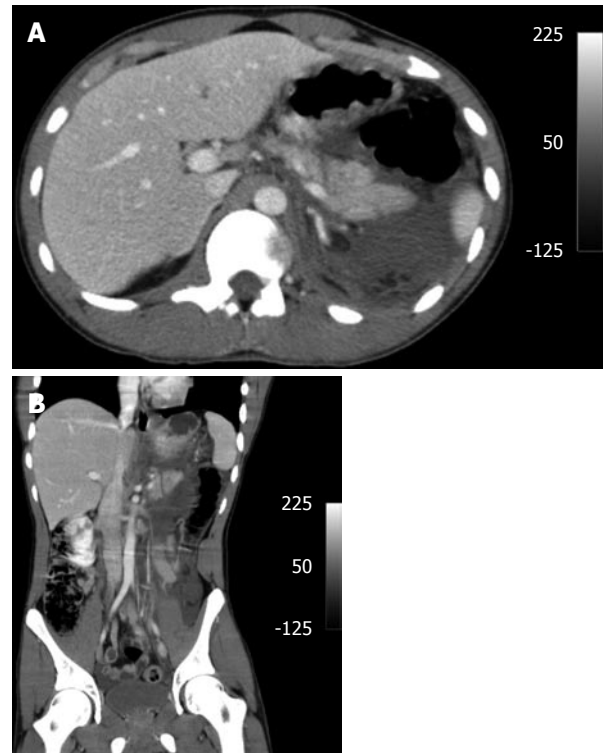


Figure 1 Abdominal computed tomography showing a pancreas fracture and fluid in the upper abdomen.

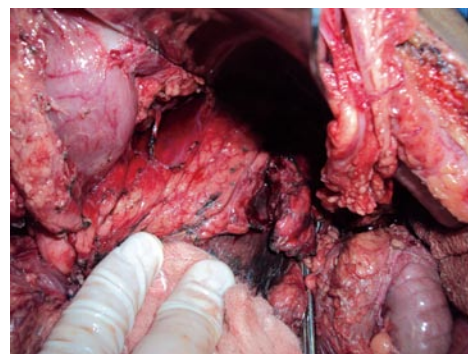


Figure 2 Pancreas fracture.



Figure 3 Final aspect.

diagnosis is imperative so that treatment can be offered as soon as possible.

CT has a low accuracy for diagnosis of pancreatic injury<sup>[15]</sup>, with acceptable sensitivity ranging from 68%–71.4%<sup>[13,16,17]</sup>. Detecting major injury with CT is difficult, with low accuracy<sup>[1]</sup>. Findings on CT which may indicate pancreatic injury are intra/extra peritoneal fluid, fluid in the lesser sac, thickening of the left anterior renal fascia and, the most important one, fluid between the splenic vein and the pancreas, seen in 90% of cases. Findings on CT can be normal, despite the presence of duct disruption<sup>[15]</sup>. If transection of the pancreas is complete or laceration seen on CT is more than half of the organ, major duct injury should be suspected and surgery scheduled<sup>[3]</sup> or endoscopic retrograde pancreatography (ERP) performed if suitable. Besides CT, ERP and magnetic resonance pancreatography (MRP) can be performed. Since mortality and morbidity is strongly related to major duct injury, its integrity should be assessed. ERP can easily do this but is rarely available at the time of the trauma and only a few patients are suitable for the exam<sup>[3,17]</sup>. MRP is more available and easier to perform<sup>[3]</sup>. Another useful tool of ERP is ductal stenting. Lin *et al.*<sup>[3]</sup> showed that the procedure helps in the management of pancreatic fistula but may be complicated by long term strictures. Attention must also be paid because stenting in the acute phase may lead to delay in necessary surgical and definitive treatment.

Surgery may be needed in almost all cases during the course of recovery. It may be indicated at admission or some time later to correct possible strictures. Choosing the right procedure depends on the extent of the injury and the presence or not of associated injuries. When distal duct disruption is present, pancreatic resection should be performed<sup>[3]</sup>; for proximal duct injury, closed suction drainage and distal resection can be selected, with duct stenting an option. A study from Taiwan showed that DP is a superior operative treatment for distal injuries when compared to pancreaticojejunostomy, which had a high complication rate of 60% due to anastomotic leakage<sup>[3]</sup>. The literature agrees that pancreatic fistula is responsible for high rates of morbidity and mortality in this kind of trauma, especially with delayed diagnosis<sup>[1,3,11,12]</sup>.

When DP is indicated and there are no associated injuries, a controversial matter comes up: to preserve the spleen or not. Authors who advocate DP with splenectomy claim that this procedure increases blood loss, surgical time and demands great surgical skills. A small study with 40 patients conducted by Benoist in France suggested a better postoperative course when splenectomy is performed. He found significant differences in postoperative complications between the procedures for pancreatic fistula (12% *vs* 40%,  $P < 0.05$ ) and subphrenic abscesses (4% *vs* 27%,  $P < 0.05$ ), more frequent after spleen preservation. Due to this, hospital stay was longer in the preservation group. Despite their findings, they could not explain the difference in the rate of pancreatic fistula between the procedures<sup>[5]</sup>. Another possible disadvantage is that the displacement of the spleen may lead to an inherent risk of torsion or hemorrhage<sup>[6]</sup>.

On the other hand, many authors accept and advocate the spleen preserving procedure<sup>[4,6,7,9-12]</sup>. The first ones to study and compare these two procedures and to favor spleen preservation were Richardson *et al.*<sup>[17]</sup> and Aldridge *et al.*<sup>[18]</sup>. Both groups consider DP with spleen preservation a safe and feasible procedure. Lin *et al.*<sup>[3]</sup> found a 22% complication rate for spleen preserving against 72.7% for the splenectomy procedure ( $P < 0.05$ ). The higher complication rate was, according to the authors, due to associated injuries, but not confirmed by others.

Shoup *et al.*<sup>[12]</sup> discussed the main reasons for splenectomy: blood loss and surgical time. Patients whose spleen were preserved had less blood loss (350 mL *vs* 600 mL,  $P < 0.01$ ). Surgical time tended to be longer in the splenectomy group, although significant difference was not reached. Another statistically significant finding was the incidence of infection; spleen preservation carried a 9% rate *vs* 28% in the splenectomy group ( $P = 0.07$ ). In addition, complications in the latter group were more severe ( $P = 0.05$ ), with an increased hospital stay ( $P < 0.01$ ).

Carrère *et al.*<sup>[11]</sup> also support the spleen preserving procedure. When splenectomy was performed, they found a significant difference for developing postoperative complications (13% *vs* 34%,  $P = 0.03$ ), intra-abdominal infected collections (3% *vs* 18%,  $P = 0.02$ ), infectious complications (8% *vs* 32%,  $P = 0.03$ ). More reoperations were required in these patients, but this did not reach statistical significance. An interesting fact is that it did not happen due to associated injuries ( $P = 0.53$ ). Univariate analysis showed that splenectomy was the only risk factor for postoperative complications (odds ratio: 3.2, 95% confidence interval: 1.1–10.2,  $P = 0.04$ ).

Another study from Singapore<sup>[10]</sup> with 232 patients showed that splenectomy was associated with an increased risk of developing pancreatic fistula and non pancreatic fistula related complications. On univariate analysis, splenectomy was significantly associated with non pancreatic fistula related complications ( $P = 0.049$ ). They suggest that splenic preservation does not decrease the occurrence of pancreatic fistula but may protect against its progression to infectious complications<sup>[10]</sup>.

The same opinion is shared by Rodríguez *et al.*<sup>[7]</sup>. In their paper, patients who had their spleen preserved had less blood loss ( $P < 0.0001$ ), shorter operative time ( $P < 0.0001$ ) and shorter hospitalization ( $P < 0.0001$ ), consistent with other findings<sup>[10,12]</sup>. These factors were significant predictors of postoperative complications. Another issue discussed was that macroscopic inspection of the spleen is reliable, as mentioned in other papers<sup>[7,11]</sup>, although some changes in the organ's color may occur<sup>[7]</sup>.

In conclusion, our group believe that DP with spleen preservation is feasible and safe. Although it is mentioned in the literature as a debatable matter, the majority of papers favor spleen preservation, with a decreased risk of complications and good outcomes. We also suggest that the spleen preserving procedure be done whenever possible.

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





## ACKNOWLEDGMENTS

## Acknowledgments to reviewers of *World Journal of Gastrointestinal Surgery*

Many reviewers have contributed their expertise and time to the peer review, a critical process to ensure the quality of *World Journal of Gastrointestinal Surgery*. 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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January 26-30, 2011

5th UK Alpine Liver and Pancreatic  
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February 01-03, 2011

6th Annual Academic Surgical  
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Minimally Invasive Surgery  
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British Society for Gastroenterology  
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March 25-27, 2011

NZAGS Conference 2011 GI Surgery,  
New Plymouth, New Zealand

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Gastrointestinal and Endoscopic  
Surgeons 2011 Annual Meeting, San  
Antonio Convention Center, San  
Antonio, TX, United States

April 02-06, 2011

The American Association for  
Cancer Research 102nd Annual  
Meeting, Orlando, FL, United States

April 10-12, 2011

The American Association of  
Endocrine Surgeons 32nd Annual  
Meeting, Houston, TX, United States

April 14-16, 2011

The American Surgical Association  
131st Annual Meeting, Boca Raton,  
FL, United States

May 07-10, 2011

Digestive Disease Week, Chicago,  
IL, United States

May 07-10, 2011

45th Annual Meeting of the Pancreas  
Club, Chicago, IL, United States

June 15-18, 2011

19th International Congress of  
the European Association for  
Endoscopic Surgery, in collaboration  
with and incorporating the 15th  
National Congress of the Italian  
Society of Endoscopic Surgery,  
Torino, Italy

September 10-14, 2011

International Congress of  
Endoscopy, Los Angeles, CA,

United States

September 22-24, 2011

5th joint EAES and ESGE, European  
Workshop on NOTES, Frankfurt,  
Germany

September 23-25, 2011

The New England Surgical Society  
92nd Annual Meeting, Breton  
Woods, NH, United States

September 23-27, 2011

ECCO-European Society for Medical  
Oncology Congress, Stockholm,  
Sweden

October 23-27, 2011

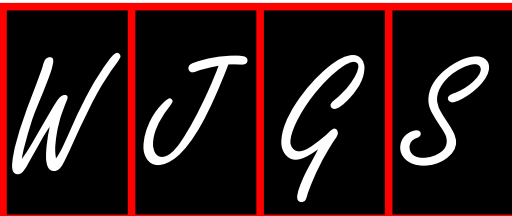
The American College of Surgeons  
97th Annual Clinical Congress, San  
Francisco, CA, United States

November 02-05, 2011

American Pancreatic Association  
42nd Annual Meeting, Chicago, IL,  
United States

November 13-16, 2011

The Western Surgical Association  
119th Scientific Session, Tucson, AZ,  
United States



## INSTRUCTIONS TO AUTHORS

### GENERAL INFORMATION

*World Journal of Gastrointestinal Surgery* (*World J Gastrointest Surg*, *WJGS*, online ISSN 1948-9366, DOI: 10.4240), is a monthly, open-access (OA), peer-reviewed journal supported by an editorial board of 336 experts in gastrointestinal surgery from 35 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 *WJGS* 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 *WJGS* is an open-access journal, readers around the world can immediately download and read, free of charge, high-quality, peer-reviewed articles from *WJGS* 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,

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The major task of *WJGS* is to rapidly report the most recent results in basic and clinical research on gastrointestinal surgery, specifically including micro-invasive surgery, laparoscopy, hepatic surgery, biliary surgery, pancreatic surgery, splenic surgery, surgical nutrition, portal hypertension, as well as the associated subjects such as epidemiology, cancer research, biomarkers, prevention, pathology, radiology, genetics, genomics, proteomics, pharmacology, pharmacokinetics, pharmacogenetics, molecular biology, clinical trials, diagnosis and therapeutics and multimodality treatment. Emphasis is placed on original research articles and clinical case reports. This journal will also provide balanced, extensive and timely review articles on selected topics.

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The columns in the issues of *WJGS* will include: (1) Editorial: To introduce and comment on major advances and developments in the field; (2) Frontier: To review representative achievements, comment on the state of current research, and propose directions for future research; (3) Topic Highlight: This column consists of three formats, including (A) 10 invited review articles on a hot topic, (B) a commentary on common issues of this hot topic, and (C) a commentary on the 10 individual articles; (4) Observation: To update the development of old and new questions, highlight unsolved problems, and provide strategies on how to solve the questions; (5) Guidelines for Basic Research: To provide guidelines for basic research; (6) Guidelines for Clinical Practice: To provide guidelines for clinical diagnosis and treatment; (7) Review: To review systemically progress and unresolved problems in the field, comment on the state of current research, and make suggestions for future work; (8) Original Article: To report innovative and original findings in gastrointestinal surgery; (9) Brief Article: To briefly report the novel and innovative findings in gastrointestinal surgery; (10) Case Report: To report a rare or typical case; (11) Letters to the Editor: To discuss and make reply to the contributions published in *WJGS*, or to introduce and comment on a controversial issue of general interest; (12) Book Reviews: To introduce and comment on quality monographs of gastrointestinal surgery; and (13) Guidelines: To introduce consensus and guidelines reached by international and national academic authorities worldwide on basic research and clinical practice in gastrointestinal surgery.

#### Name of journal

*World Journal of Gastrointestinal Surgery*

#### ISSN

ISSN 1948-9366 (online)

#### Indexing/abstracting

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## SPECIAL STATEMENT

All articles published in this journal represent the viewpoints of the authors except where indicated otherwise.

### Biostatistical editing

Statistical review is performed after peer review. We invite an expert in Biomedical Statistics from to evaluate the statistical method used in the paper, including *t*-test (group or paired comparisons), chi-squared test, Redit, probit, logit, regression (linear, curvilinear, or stepwise), correlation, analysis of variance, analysis of covariance, *etc.* The reviewing points include: (1) Statistical methods should be described when they are used to verify the results; (2) Whether the statistical techniques are suitable or correct; (3) Only homogeneous data can be averaged. Standard deviations are preferred to standard errors. Give the number of observations and subjects (*n*). Losses in observations, such as drop-outs from the study should be reported; (4) Values such as ED50, LD50, IC50 should have their 95% confidence limits calculated and compared by weighted probit analysis (Bliss and Finney); and (5) The word 'significantly' should be replaced by its synonyms (if it indicates extent) or the *P* value (if it indicates statistical significance).

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In the interests of transparency and to help reviewers assess any potential bias, *WJGS* requires authors of all papers to declare any competing commercial, personal, political, intellectual, or religious interests in relation to the submitted work. Referees are also asked to indicate any potential conflict they might have reviewing a particular paper. Before submitting, authors are suggested to read "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Ethical Considerations in the Conduct and Reporting of Research: Conflicts of Interest" from International Committee of Medical Journal Editors (ICMJE), which is available at: [http://www.icmje.org/ethical\\_4conflicts.html](http://www.icmje.org/ethical_4conflicts.html).

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Manuscripts should contain a statement to the effect that all human studies have been reviewed by the appropriate ethics committee or it should be stated clearly in the text that all persons gave their informed consent prior to their inclusion in the study. Details that might disclose the identity of the subjects under study should be omitted. Authors should also draw attention to the Code of Ethics of the World Medical Association (Declaration of Helsinki, 1964, as revised in 2004).

### Statement of human and animal rights

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Authors should retain one copy of the text, tables, photographs and illustrations because rejected manuscripts will not be returned to the author(s) and the editors will not be responsible for loss or damage to photographs and illustrations sustained during mailing.

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**Title:** Title should be less than 12 words.

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**Author contributions:** The format of this section should be: Author contributions: Wang CL and Liang L contributed equally to this work; Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed the data; and Wang CL, Liang L and Fu JF wrote the paper.

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### Abstract

There are unstructured abstracts (no more than 256 words) and structured abstracts (no more than 480). The specific requirements for structured abstracts are as follows:

An informative, structured abstracts of no more than 480 words should accompany each manuscript. Abstracts for original contributions should be structured into the following sections. AIM (no more than 20 words): Only the purpose should be included. Please write the aim as the form of "To investigate/study/..."; MATERIALS AND METHODS (no more than 140 words); RESULTS (no more than 294 words): You should present *P* values where appropriate and must provide relevant data to illustrate how they were obtained, e.g.  $6.92 \pm 3.86$  vs  $3.61 \pm 1.67$ ,  $P < 0.001$ ; CONCLUSION (no more than 26 words).

### Key words

Please list 5-10 key words, selected mainly from *Index Medicus*,

which reflect the content of the study.

### Text

For articles of these sections, original articles and brief articles, the main text should be structured into the following sections: INTRODUCTION, MATERIALS AND METHODS, RESULTS and DISCUSSION, and should include appropriate Figures and Tables. Data should be presented in the main text or in Figures and Tables, but not in both. The main text format of these sections, editorial, topic highlight, case report, letters to the editors, can be found at: [http://www.wjgnet.com/1948-9366/g\\_info\\_list.htm](http://www.wjgnet.com/1948-9366/g_info_list.htm).

### Illustrations

Figures should be numbered as 1, 2, 3, *etc.*, and mentioned clearly in the main text. Provide a brief title for each figure on a separate page. Detailed legends should not be provided under the figures. This part should be added into the text where the figures are applicable. Figures should be either Photoshop or Illustrator files (in tiff, eps, jpeg formats) at high-resolution. Examples can be found at: <http://www.wjgnet.com/1007-9327/13/4520.pdf>; <http://www.wjgnet.com/1007-9327/13/4554.pdf>; <http://www.wjgnet.com/1007-9327/13/4891.pdf>; <http://www.wjgnet.com/1007-9327/13/4986.pdf>; <http://www.wjgnet.com/1007-9327/13/4498.pdf>. Keeping all elements compiled is necessary in line-art image. Scale bars should be used rather than magnification factors, with the length of the bar defined in the legend rather than on the bar itself. File names should identify the figure and panel. Avoid layering type directly over shaded or textured areas. Please use uniform legends for the same subjects. For example: Figure 1 Pathological changes in atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...*etc.* It is our principle to publish high resolution-figures for the printed and E-versions.

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Three-line tables should be numbered 1, 2, 3, *etc.*, and mentioned clearly in the main text. Provide a brief title for each table. Detailed legends should not be included under tables, but rather added into the text where applicable. The information should complement, but not duplicate the text. Use one horizontal line under the title, a second under column heads, and a third below the Table, above any footnotes. Vertical and italic lines should be omitted.

### Notes in tables and illustrations

Data that are not statistically significant should not be noted. <sup>a</sup>*P* < 0.05, <sup>b</sup>*P* < 0.01 should be noted (*P* > 0.05 should not be noted). If there are other series of *P* values, <sup>c</sup>*P* < 0.05 and <sup>d</sup>*P* < 0.01 are used. A third series of *P* values can be expressed as <sup>e</sup>*P* < 0.05 and <sup>f</sup>*P* < 0.01. Other notes in tables or under illustrations should be expressed as <sup>1</sup>F, <sup>2</sup>F, <sup>3</sup>F; or sometimes as other symbols with a superscript (Arabic numerals) in the upper left corner. In a multi-curve illustration, each curve should be labeled with ●, ○, ■, □, ▲, △, *etc.*, in a certain sequence.

### Acknowledgments

Brief acknowledgments of persons who have made genuine contributions to the manuscript and who endorse the data and conclusions should be included. Authors are responsible for obtaining written permission to use any copyrighted text and/or illustrations.

## REFERENCES

### Coding system

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example, "From references<sup>[19,22-24]</sup>, we know that..."

When the authors write the references, please ensure that the order in text is the same as in the references section, and also ensure the spelling accuracy of the first author's name. Do not list the same citation twice.

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### Format

#### Journals

*English journal article (list all authors and include the PMID where applicable)*

- 1 **Jung EM**, Clevert DA, Schreyer AG, Schmitt S, Rennert J, Kubale R, Feuerbach S, Jung F. Evaluation of quantitative contrast harmonic imaging to assess malignancy of liver tumors: A prospective controlled two-center study. *World J Gastroenterol* 2007; **13**: 6356-6364 [PMID: 18081224 DOI: 10.3748/wjg.13.6356]

*Chinese journal article (list all authors and include the PMID where applicable)*

- 2 **Lin GZ**, Wang XZ, Wang P, Lin J, Yang FD. Immunologic effect of Jianpi Yishen decoction in treatment of Pixu-diarhoea. *Shijie Huaren Xiaobua Zazhi* 1999; **7**: 285-287

*In press*

- 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

*Organization as author*

- 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]

*Both personal authors and an organization as author*

- 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]

*No author given*

- 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]

*Volume with supplement*

- 7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/

j.1526-4610.42.s2.7.x]

*Issue with no volume*

- 8 **Banit DM**, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res* 2002; (**401**): 230-238 [PMID: 12151900 DOI:10.1097/00003086-200208000-00026]

*No volume or issue*

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

### Books

*Personal author(s)*

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

*Chapter in a book (list all authors)*

- 11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

*Author(s) and editor(s)*

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

*Conference proceedings*

- 13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

*Conference paper*

- 14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

**Electronic journal** (list all authors)

- 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/cid/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

### Statistical data

Write as mean  $\pm$  SD or mean  $\pm$  SE.

### Statistical expression

Express *t* test as *t* (in italics), *F* test as *F* (in italics), chi square test as  $\chi^2$  (in Greek), related coefficient as *r* (in italics), degree of freedom as *v* (in Greek), sample number as *n* (in italics), and probability as *P* (in italics).

### Units

Use SI units. For example: body mass, *m* (B) = 78 kg; blood pressure, *p* (B) = 16.2/12.3 kPa; incubation time, *t* (incubation) = 96 h; blood glucose concentration, *c* (glucose)  $6.4 \pm 2.1$  mmol/L; blood CEA mass concentration, *p* (CEA) =  $8.6 \pm 24.5$   $\mu$ g/L; CO<sub>2</sub> volume fraction, 50 mL/L CO<sub>2</sub>, not 5% CO<sub>2</sub>; likewise for 40 g/L formaldehyde, not 10% formalin; and mass fraction, 8 ng/g, etc. Arabic numerals such as 23, 243, 641 should be read 23 243 641.

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### Abbreviations

Standard abbreviations should be defined in the abstract and on first mention in the text. In general, terms should not be abbreviated unless they are used repeatedly and the abbreviation is helpful to the reader. Permissible abbreviations are listed in Units, Symbols



and Abbreviations: A Guide for Biological and Medical Editors and Authors (Ed. Baron DN, 1988) published by The Royal Society of Medicine, London. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, mAb, can be used directly without further explanation.

### Italics

Quantities: *t* time or temperature, *c* concentration, *A* area, *l* length, *m* mass, *V* volume.

Genotypes: *gyrA*, *arg 1*, *c myc*, *c fos*, etc.

Restriction enzymes: *EcoRI*, *HindII*, *BamHI*, *Kho I*, *Kpn I*, etc.

Biology: *H. pylori*, *E. coli*, etc.

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**Editorial:** [http://www.wjgnet.com/1948-9366/g\\_info\\_20100312190249.htm](http://www.wjgnet.com/1948-9366/g_info_20100312190249.htm)

**Frontier:** [http://www.wjgnet.com/1948-9366/g\\_info\\_20100312190321.htm](http://www.wjgnet.com/1948-9366/g_info_20100312190321.htm)

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