

WJG 20th Anniversary Special Issues (8): Gastric cancer

Problems faced by evidence-based medicine in evaluating lymphadenectomy for gastric cancer

Giuseppe Verlato, Simone Giacomuzzi, Maria Bencivenga, Paolo Morgagni, Giovanni De Manzoni

Giuseppe Verlato, Unit of Epidemiology and Medical Statistics, Department of Public Health and Community Medicine, University of Verona, 37134 Verona, Italy

Simone Giacomuzzi, Maria Bencivenga, Giovanni De Manzoni, Unit of Upper GI Surgery, University of Verona, 37126 Verona, Italy

Paolo Morgagni, Gastrointestinal and General Surgery Unit, Morgagni-Pierantoni Hospital, 47121 Forlì, Italy

Author contributions: Verlato G, Giacomuzzi S, Bencivenga M, Morgagni P and De Manzoni G solely contributed to this paper.

Correspondence to: Giovanni De Manzoni, MD, Unit of Upper GI Surgery, University of Verona, OCM Borgo Trento, Piazzale Stefani 1, 37126 Verona, Italy. giovanni.demanzoni@univr.it
Telephone: +39-45-8123063 Fax: +39-45-8122484

Received: October 29, 2013 Revised: March 4, 2014

Accepted: April 15, 2014

Published online: September 28, 2014

Abstract

Gastric cancer surgical management differs between Eastern Asia and Western countries. Extended lymphadenectomy (D2) is the standard of care in Japan and South Korea since decades, while the majority of United States patients receive at most a limited lymphadenectomy (D1). United States and Northern Europe are considered the scientific leaders in medicine and evidence-based procedures are the cornerstone of their clinical practice. However, surgeons in Eastern Asia are more experienced, as there are more new cases of gastric cancer in Japan (107898 in 2012) than in the entire European Union (81592), or in South Korea (31269) than in the entire United States (21155). For quite a long time evidence-based medicine (EBM) did not solve the question whether D2 improves long-term prognosis with respect to D1. Indeed, eastern surgeons were reluctant to perform D1 even in the frame of a clinical trial, as their patients had a very good prognosis after D2. Evidence-based surgical indications provided by Western trials were questioned, as surgical procedures could not be properly standardized. In the present study

we analyzed indications about the optimal extension of lymphadenectomy in gastric cancer according to current scientific literature (2008-2012) and surgical guidelines. We searched PubMed for papers using the key words "lymphadenectomy or D1 or D2" AND "gastric cancer" from 2008 to 2012. Moreover, we reviewed national guidelines for gastric cancer management. The support to D2 lymphadenectomy increased progressively from 2008 to 2012: since 2010 papers supporting D2 have achieved a higher overall impact factor than the other papers. Till 2011, D2 was the procedure of choice according to experts' opinion, while three meta-analyses found no survival advantage after D2 with respect to D1. In 2012-2013, however, two meta-analyses reported that D2 improves prognosis with respect to D1. D2 lymphadenectomy was proposed as the standard of care for advanced gastric cancer by Japanese National Guidelines since 1981 and was adopted as the standard procedure by the Italian Research Group for Gastric Cancer since the Nineties. D2 is now indicated as the standard of surgical treatment with curative intent by the German, British and ESMO-ESSO-ESTRO guidelines. At variance American NCCN guidelines recommend a D1⁺ or a modified D2 lymph node dissection. In conclusion, D2 lymphadenectomy, originally developed by Eastern surgeons, is now becoming the procedure of choice also in the West. In gastric cancer surgery EBM is lagging behind national guidelines, rather than preceding and orienting them. To eliminate this lag, EBM should value to a larger extent Eastern Asian literature and should evaluate not only the quality of the study design but also the quality of surgical procedures.

© 2014 Baishideng Publishing Group Inc. All rights reserved.

Key words: Gastric cancer; Surgical quality; Lymphadenectomy; Evidence-based medicine; National guidelines; Eastern Asia; United States

Core tip: The extension of lymphadenectomy in advanced gastric cancer has been debated for several

decades. Till recently Western surgeons supported limited lymphadenectomy in agreement with a Cochrane review and several meta-analyses, while Japanese surgeons preferred the extended procedure. Nowadays extended lymphadenectomy is considered the procedure of choice by most national guidelines. In gastric cancer surgery evidence-based medicine (EBM) is lagging behind national guidelines, rather than preceding and orienting them. To eliminate this lag, EBM should value to a larger extent Eastern Asian literature and should evaluate not only the quality of the study design but also the quality of surgical procedures.

Verlato G, Giacomuzzi S, Bencivenga M, Morgagni P, De Manzoni G. Problems faced by evidence-based medicine in evaluating lymphadenectomy for gastric cancer. *World J Gastroenterol* 2014; 20(36): 12883-12891 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v20/i36/12883.htm> DOI: <http://dx.doi.org/10.3748/wjg.v20.i36.12883>

HISTORICAL PERSPECTIVE

Eastern-Western discrepancies in gastric cancer surgery

Gastric cancer surgery differs between Eastern Asia and the United States. Extended lymphadenectomy (D2) has been the standard of care for advanced gastric cancer in Japan and South Korea since decades^[1-3], while the majority of patients in the United States receive at most a limited lymphadenectomy (D1) followed by post-operative chemoradiation^[4]. This difference is even more striking, if one considers that Japanese surgeons had extended lymphadenectomy to para-aortic nodes (D3 procedure), until a randomized controlled trial showed no survival advantage with respect to D2 procedure^[5]. On the contrary, in the United States less than a D1 lymphadenectomy has been performed in a substantial proportion, or even in the majority of patients such as in the Intergroup 0116 trial^[6].

Western countries are the leaders in medical research

United States and Northern European countries are considered the scientific leaders in medicine: indeed the most important medical journals are published in the United States [*New Engl J Med*, impact factor (IF) in 2012 = 51.658; *Science*, IF = 31.027] or in England (*Lancet*, IF = 39.060; *Nature*, IF = 38.597).

Evidence-based procedures are the cornerstone of clinical practice in Western countries. Anyway, due to the difficulty in standardizing surgical procedures, evidence-based surgical indications may not be unquestionable. The extent of lymphadenectomy in surgical management of gastric cancer proves this point.

Indeed the Western surgical approach to advanced gastric cancer was supported by a Cochrane review published in 2003^[7] and 2005^[8], reporting that “randomised studies show no evidence of overall survival benefit” after D2 dissection, “but possible benefit in T3 tumors.” These conclusions were mainly based on the results of a

Dutch^[9] and a British^[10] trials, showing that D2 provided no 5-year survival advantage with respect to D1. Of note, the Cochrane review acknowledged that “these results may be confounded by surgical learning curves and poor surgeon compliance”^[8].

However it was acknowledged that D2 lymphadenectomy was necessary to harvest at least 15 lymph nodes, *i.e.*, to adequately stage tumours^[11,12]. To circumvent this problem, nodal invasion was evaluated not only by N status but also by N ratio^[13,14].

While eastern countries have the largest surgical experience

On the other hand, surgeons in Eastern Asia are more experienced, as there are more new cases of gastric cancer in Japan (107898 in 2012) than in the 28 countries of the European Union (81592), or in South Korea (31269) than in the entire United States (21155)^[15] (Figure 1).

Indeed Eastern surgeons achieve better short-term results than their Western counterparts (Table 1)^[16]. Of note, the two trials on which the Cochrane review was based^[17,18] had been carried out by surgeons without previous training in extended lymphadenectomy, doing less than 5 five interventions per year. The limited surgical experience yielded a very high post-operative mortality after extended lymphadenectomy (9.7% in the Dutch trial and 13.5% in the British trial), a high percentage of splenectomies (37% and 65%, respectively) and pancreatectomies (30% and 56%) and a low number of retrieved nodes (median of 17 nodes in the British trial)^[19]. By comparison, at the same time, mortality after D2 dissection was less than 2% in the nationwide Japanese registry^[20]; likewise in a Japanese trial mortality after D2 was less than 1% and the median number of retrieved nodes was 54^[21]. Of note, in the Dutch trial D2 was associated with an increased long-term survival with respect to D1 when excluding post-operative mortality ($P = 0.02$)^[22].

In the meantime another randomized trial, performed in Taiwan^[23], showed a mild but significant survival advantage after D2 with respect to D1; 5-year survival was 59.5% and 53.6%, respectively ($P = 0.041$); interestingly, none of the patients recruited died in the post-operative period^[24]. Of note, a clinical trial comparing D1 and D2 could not be devised in Japan at that time, as the two procedures were not in equipoise according to Japanese surgeons. The Japan Clinical Oncology Group instead performed a trial to compare D2 and D3 lymphadenectomies^[5].

In the Eastern-Western debate on gastric cancer, the Eastern position is considerably strengthened by the impressive long-term survival of Eastern patients: overall 5-year survival achieved values of 68%-74% in Japanese gastric cancer patients^[2,25] whereas in Europe during the 1990s survival was three-fold lower (24%)^[26].

Italian Research Group for Gastric Cancer between the East and the West

Of note, the GIRCG (Gruppo Italiano per la Ricerca sul Cancro Gastrico-Italian Research Group for Gastric Cancer) gave an important contribution to the debate on the



Figure 1 New cases of gastric cancer in 2012 in the West and in the East, according to GLOBOCAN 2012^[15].

Table 1 Short-term results of gastric cancer surgery with D2 lymphadenectomy in Eastern Asia *vs* Europe, in clinical trials *vs* observational studies^[16]

	Post-operative mortality	Post-operative morbidity	Median nodes retrieved	Adequate staging (≥ 15 nodes)
Eastern Asia				
Trials	0%-0.8%	17%-21%	54	100%
Observational	< 2%	-	-	-
Europe				
Trials	5%-14%	43%-46%	17	-
Observational	2%-5%	21%-35%	25-26	86%-95%
IRGGC (VR, SL, PD)	3.6%	33.6%	29 (IQ 21-38)	93.8%

IRGGC: Italian Research Group for Gastric Cancer.

extension of lymphadenectomy for gastric cancer.

First of all the GIRCG showed that D2 dissection is feasible on western patients with acceptable mortality and morbidity (2% and 17% respectively) rates and provides 32% probability of 5-year survival, even for patients with involvement of regional lymph nodes^[27].

In 2005 De Manzoni and Verlato^[28] criticized the Cochrane review on gastric cancer surgery^[8] (later withdrawn^[29]) for not taking into account the Japanese literature. Indeed in the past the British and American physicians gave a fundamental contribution to understanding even diseases which were rare in their countries: for instance, beta thalassemia was named Cooley's anemia after the American physician who first described the disease in immigrant Italian children with characteristic anemia and bone deformities^[30]. However, nowadays scientific

methodology has spread to several countries^[31], so that the leading countries in a particular medical field are often those with the highest incidence, such as Japan and South Korea for gastric cancer. Indeed "it is extremely difficult to ask Japanese surgeons, in whose series postoperative mortality is only 1%-2%, to believe in randomized clinical trials where postoperative mortality peaks to 10%-14%, irrespectively of methodological quality of those studies^[16].

In 2009 Verlato *et al*^[16] pointed out that "in this third millennium, papers dealing with surgery for gastric cancer cannot be evaluated only according to the quality of the study design, such as the Jadad score, but also the quality of surgical procedures must be taken into account". To overcome this problem Verlato *et al*^[16] proposed indexes of surgical quality (number of retrieved nodes, percentage of splenectomy and splenopancreasectomy, postoperative morbidity, and in-hospital mortality). Indeed, the learning curve, standardization of the procedures, poor surgical performances are among the main difficulties related to RCTs in the surgical field. Also randomization can be hampered by ethical issues, emergency setting, or need of palliative care, while patients' and surgeons' equipoise can be more difficult to achieve than in the medical field^[32].

COMPARISON OF NATIONAL GUIDELINES AND CURRENT SCIENTIFIC RESEARCH

Extension of lymphadenectomy recommended by national guidelines

D2 was adopted as the standard of surgical treatment with curative intent by the Japanese^[1,2,25,33], German^[34,35]

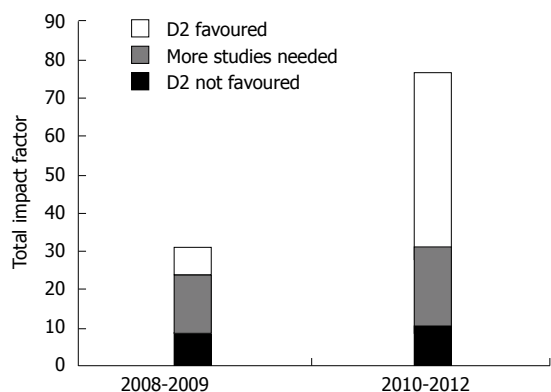


Figure 2 Overall Impact Factor of articles, classified as a function of D1/D2 preferences (D1 favoured, more studies needed, D2 favoured) and time (2008/09 vs 2010/12).

and British^[36] national guidelines, by the European Society for Medical Oncology (ESMO) guidelines^[37], by the joint ESMO - European Society of Surgical Oncology (ESSO) - European Society of Radiotherapy and Oncology (ESTRO) guidelines^[38]. The ESMO-ESSO-ESTRO guidelines ranked the level of evidence as the highest (I) and the grade of recommendation as B (strong or moderate evidence for efficacy but with a limited clinical benefit)^[38]. Of note, D2 is recommended by the Japanese guidelines since 1981^[1] and by German guidelines since at least 2005^[34], and D2 was adopted as the preferred lymphadenectomy within the Italian Research Group for Gastric Cancer (GIRCG) since 1992^[16,27]. At variance American NCCN guidelines recommend a D1+ or a modified D2 lymph node dissection, the latter performed by experienced surgeons in high-volume centers^[39].

Optimal extension of lymphadenectomy according to current scientific literature (2008-2012)

We searched PubMed for papers using the key words “lymphadenectomy or D1 or D2” AND “gastric cancer”, published in English language between 2008 and 2012. The year 2013 was not included in the systematic review, as the articles published in this year were still being introduced in medical databases which are updated with some delay. The search was limited to full-length articles in English language. In addition, bibliographies were manually inspected, to identify the relevant publications for possible inclusion.

Potentially relevant studies ($n = 1174$) were identified and screened for retrieval. Letters and commentaries were excluded; when duplicate articles on the same series were found, only the most recent was considered. A total of 45 full-length articles, comparing short and/or long-term effectiveness of either lymphadenectomies, were considered, 5 supporting D1, 25 supporting D2, and 15 underlying the need for further studies. Of these, 35 articles had been published on journals indexes by the Journal Citation Reports, 13 pointing out the need for further studies^[40-52], 5 favouring D1^[53-57], 17 supporting D2^[58-74] (Table 2). Interestingly no article published on journals

without impact factor was in favour of D1 lymphadenectomy, while 8 supported D2^[75-82] and 2 underlined the need for more studies^[83-84].

As shown in Figure 2 and in Table 2^[40-74], the support to D2 lymphadenectomy increased progressively during the study period: since 2010 papers supporting D2 have achieved a higher overall IF than the other papers.

Initially D2 was indicated as the procedure of choice mainly by review articles and papers conveying expert opinion, while three meta-analyses^[53,55,56], published between 2008 and 2011, reported that extended lymphadenectomy does not offer benefit over limited lymphadenectomy. However, in 2012 D2 was indicated as the procedure of choice in advanced gastric cancer also by a meta-analysis^[73]. “Earlier trials show that D2 dissections have higher operative mortality, while recent trials have similar rates. A trend of improved survival exists among D2 patients who did not undergo resection of the spleen or pancreas, as well as for patients with T3/T4 cancers”^[73].

Also the authors of the Dutch trial, after considering the 15-year follow-up results, concluded that: “Considering that a safer, spleen-preserving D2 resection is currently available in high-volume centres, and our findings of better recurrence and gastric-cancer-related survival rates, D2 resection now seems likely to be the recommended surgical approach for patients with resectable (curable) gastric cancer, despite the earlier follow-up results”^[65].

The authors of another clinical trial performed in Italy^[47] reported that patients undergoing D1 or D2 experienced similar post-operative morbidity (12% and 17.9% respectively) and mortality (3% and 2.2%) and concluded that “D2 dissection, in an appropriate setting, can therefore be considered a safe option for the radical management of gastric cancer in Western patients”.

In the era of tailored treatment, other Authors suggested to move “away from the D2 versus D1 debate” and to choose the extension of lymphadenectomy according to “the stage of the cancer and the age and fitness of the patient”^[85]. Similarly, an expert panel, using the RAND/UCLA appropriateness methodology, concluded that “a D2 lymphadenectomy is preferred for curative-intent resection in advanced, nonmetastatic GC; and in patients with early GC or substantial comorbidities, a D1 lymphadenectomy is more appropriate”^[86].

CONCLUSION

Towards an international agreement?

EBM, which till recently has not reported any advantage of extended D2 lymphadenectomy with respect to the limited D1 procedure^[7,8,53,55,56], is now supporting D2. A clinical trial performed in the East highlighted a significant 5-year survival advantage after D2 with respect to D1^[23]. A clinical trial performed on Western patients showed that D2 can be performed without excess post-operative morbidity or mortality^[47]. The most recent meta-analyses^[73,87] concluded that “D2 lymphadenectomy with spleen and pancreas preservation offers the most survival benefit”^[87].

Table 2 Summary of the systematic review of studies, comparing limited (D1) and extended (D2) lymphadenectomy and published in 2008-2012 on journals indexed by Journal Citation Reports. Articles were weighted according to 5-year impact factor (2008-2012)

Authors	Country	Journal	Year	Study design	5-yr IF
Further studies	Further studies needed				
Catalano <i>et al</i> ^[40]	Italy	<i>Crit Rev Oncol Hematol</i>	2009	Expert opinion	4.562
Coburn ^[41]	Canada	<i>J Surg Oncol</i>	2009	Review	2.710
D'souza <i>et al</i> ^[42]	India	<i>J Cancer Res Ther</i>	2009	Review	0.761 ¹
Songun <i>et al</i> ^[43]	The Netherlands	<i>Expert Rev Anticanc</i>	2009	Expert opinion	2.055
Yoon <i>et al</i> ^[44]	United States	<i>Oncologist</i>	2009	Expert opinion	5.245
Coburn ^[45]	Canada	<i>J Surg Oncol</i>	2010	Expert opinion	2.710
de Bree <i>et al</i> ^[46]	Greece	<i>J Surg Oncol</i>	2010	Review	2.710
Degiuli <i>et al</i> ^[47]	Italy	<i>Brit J Surg</i>	2010	Clinical trial	4.956
Tanizawa <i>et al</i> ^[48]	Japan	<i>Gastric Cancer</i>	2010	Review	3.615
Maduekwe <i>et al</i> ^[49]	United States	<i>J Gastrointest Surg</i>	2011	Review	2.766
Doglietto <i>et al</i> ^[50]	Italy	<i>Ann Ital Chir</i>	2012	Expert opinion	0.286
Hundahl ^[51]	United States	<i>Surg Oncol Clin N Am</i>	2012	Review	1.162
Vallbohmer <i>et al</i> ^[52]	Germany	<i>Curr Prob Surg</i>	2012	Expert opinion	2.267
Overall					35.805
D2 not favoured	D2 not favoured over D1				
Lustosa <i>et al</i> ^[53]	Brazil	<i>Acta Cir Bras</i>	2008	Meta-analysis	0.695
Van Cutsem <i>et al</i> ^[54]	EORTC ²	<i>Eur J Cancer</i>	2008	Expert opinion	5.257
Yang <i>et al</i> ^[55]	China	<i>Am J Surg</i>	2009	Meta-analysis	2.727
Memon <i>et al</i> ^[56]	Australia	<i>Ann Surg</i>	2011	Meta-analysis	8.264
Wong <i>et al</i> ^[57]	United States	<i>Curr Treat Option On</i>	2011	Expert opinion	2.422 ¹
Overall					19.365
D2 favoured	D2 favoured over D1				
Ozmen <i>et al</i> ^[58]	Turkey	<i>J Surg Oncol</i>	2008	Review	2.710
Díaz de Líaño <i>et al</i> ^[59]	Spain	<i>Clin Transl Oncol</i>	2009	Observational	1.316
Griniatsos <i>et al</i> ^[60]	Greece	<i>World J Gastroenterol</i>	2009	Observational	2.594
Kodera <i>et al</i> ^[61]	Japan	<i>Acta Chir Belg</i>	2009	Review	0.499
Roy <i>et al</i> ^[62]	India	<i>Indian J Surg</i>	2009	Review	0.092 ¹
Sasako <i>et al</i> ^[63]	Japan	<i>Jpn J Clin Oncol</i>	2010	Expert opinion	2.063
Shi <i>et al</i> ^[64]	China	<i>J Surg Oncol</i>	2010	Review	2.710
Songun <i>et al</i> ^[65]	The Netherlands	<i>Lancet Oncol</i>	2010	Clinical trial	21.856
Tentes <i>et al</i> ^[66]	Greece	<i>J BUON</i>	2010	Observational	0.653
Hussain ^[67]	United Kingdom	<i>Curr Opin Gastroen</i>	2011	Expert opinion	3.739
Meyer <i>et al</i> ^[68]	Germany	<i>Dtsch Arztebl Int</i>	2011	Expert opinion	2.988
Ott <i>et al</i> ^[69]	Germany	<i>Langenbecks Arch Surg</i>	2011	Review	1.970
Saka <i>et al</i> ^[70]	Japan	<i>Jpn J Clin Oncol</i>	2011	Review	2.063
Lee <i>et al</i> ^[71]	Korea	<i>Yonsei Med J</i>	2012	Review	1.214
Sasako ^[72]	Japan	<i>Surg Oncol Clin N Am</i>	2012	Expert opinion	1.162
Seevaratnam <i>et al</i> ^[73]	Canada	<i>Gastric Cancer</i>	2012	Meta-analysis	3.615
Viudez-Berral <i>et al</i> ^[74]	Spain	<i>Rev Esp Enferm Dig</i>	2012	Expert opinion	1.208
Overall					52.452

¹2012 impact factor was used, as the 5-year impact factor was not available; ²EORTC: European Organisation for Research and Treatment of Cancer.

for patients with advanced gastric cancer.

The latest American guidelines^[39] now include not only D1+ but also “a modified D2 lymph node dissection” among recommended procedures for patients with resectable locoregional cancer, as long as the latter is “performed by experienced surgeons in high-volume centers”.

Two American authors^[88] recently underlined that Eastern and Western surgeons are converging to consider D2 lymphadenectomy as the standard procedure, as the former have given up with super-extended procedures, while the latter “have increasingly accepted the importance of performing more than a D1 node dissection”.

Problems of EBM in gastric cancer surgery and possible solutions

In gastric cancer surgery EBM is lagging behind national

guidelines, rather than preceding and orienting them. To eliminate this lag, EBM should value to a larger extent Eastern Asian literature^[28] and should take into account not only the quality of the study design but also the quality of surgical procedures^[16].

In Western countries, where the incidence of gastric cancer is getting low, centralization of gastric cancer surgery in specialized high-volume institution would also be necessary.

As pointed out by Strong and Yoon^[88] one significant obstacle to implementing D2 lymphadenectomy in the West is the low volume of gastrectomies in Western centres. Indeed in the United States 80% of Medicare patients undergo gastrectomy in centers performing less than 20 procedures per year^[89]. This situation reflects not only the low incidence of gastric cancer in the United States but also the surgeon's habit to consider gastric sur-

gery as part of general surgery^[88].

However, several Northern European countries managed to achieve great improvements in gastric cancer surgery at national level. In the Netherlands survival of gastric cancer patients significantly improved after the implementation of the Dutch D1-D2 Gastric Cancer Trial, which involved substantial standardization and training^[90]. In Denmark 30-d hospital mortality has decreased from 8.2% to 2.4% after centralization of gastric cancer surgery and implementation of national clinical guidelines while the proportion of patients with at least 15 lymph nodes removed has increased from 19% to 76%^[91]. Centralization of gastric cancer surgery and/or audits for gastric cancer are currently implemented in the United Kingdom, Sweden, Finland, and the Netherlands^[92,93].

REFERENCES

- Kajitani T.** The general rules for the gastric cancer study in surgery and pathology. Part I. Clinical classification. *Jpn J Surg* 1981; **11**: 127-139 [PMID: 7300058 DOI: 10.1007/BF02468883]
- Maruyama K,** Kaminishi M, Hayashi K, Isobe Y, Honda I, Katai H, Arai K, Kodera Y, Nashimoto A. Gastric cancer treated in 1991 in Japan: data analysis of nationwide registry. *Gastric Cancer* 2006; **9**: 51-66 [PMID: 16767357 DOI: 10.1007/s10120-006-0370-y]
- Sasako M,** Saka M, Fukagawa T, Katai H, Sano T. Modern surgery for gastric cancer--Japanese perspective. *Scand J Surg* 2006; **95**: 232-235 [PMID: 17249270]
- Schmidt B,** Yoon SS. D1 versus D2 lymphadenectomy for gastric cancer. *J Surg Oncol* 2013; **107**: 259-264 [PMID: 22513454 DOI: 10.1002/jso.23127]
- Sasako M,** Sano T, Yamamoto S, Kurokawa Y, Nashimoto A, Kurita A, Hiratsuka M, Tsujinaka T, Kinoshita T, Arai K, Yamamura Y, Okajima K. D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. *N Engl J Med* 2008; **359**: 453-462 [PMID: 18669424 DOI: 10.1056/NEJMoa0707035]
- Hundahl SA,** Macdonald JS, Benedetti J, Fitzsimmons T; Southwest Oncology Group and the Gastric Intergroup. Surgical treatment variation in a prospective, randomized trial of chemoradiotherapy in gastric cancer: the effect of under-treatment. *Ann Surg Oncol* 2002; **9**: 278-286 [PMID: 11923135 DOI: 10.1007/BF02573066]
- McCulloch P,** Nita ME, Kazi H, Gama-Rodrigues J. Extended versus limited lymph nodes dissection technique for adenocarcinoma of the stomach. *Cochrane Database Syst Rev* 2003; **(4)**: CD001964 [PMID: 14583942 DOI: 10.1002/14651858.CD001964.pub2]
- McCulloch P,** Niita ME, Kazi H, Gama-Rodrigues JJ. Gastrectomy with extended lymphadenectomy for primary treatment of gastric cancer. *Br J Surg* 2005; **92**: 5-13 [PMID: 15635680 DOI: 10.1002/bjs.4839]
- Bonenkamp JJ,** Hermans J, Sasako M, van de Velde CJ, Welvaart K, Songun I, Meyer S, Plukker JT, Van Elk P, Obertop H, Gouma DJ, van Lanschot JJ, Taat CW, de Graaf PW, von Meyenfeldt MF, Tilanus H. Extended lymph-node dissection for gastric cancer. *N Engl J Med* 1999; **340**: 908-914 [PMID: 10089184 DOI: 10.1056/NEJM199903253401202]
- Cuschieri A,** Weeden S, Fielding J, Bancewicz J, Craven J, Joypaul V, Sydes M, Fayers P. Patient survival after D1 and D2 resections for gastric cancer: long-term results of the MRC randomized surgical trial. Surgical Co-operative Group. *Br J Cancer* 1999; **79**: 1522-1530 [PMID: 10188901 DOI: 10.1038/sj.bjc.6690243]
- de Manzoni G,** Verlato G, Roviello F, Morgagni P, Di Leo A, Saragoni L, Marrelli D, Kurihara H, Pasini F. The new TNM classification of lymph node metastasis minimises stage migration problems in gastric cancer patients. *Br J Cancer* 2002; **87**: 171-174 [PMID: 12107838 DOI: 10.1038/sj.bjc.6600432]
- Smith BR,** Stabile BE. Aggressive D2 lymphadenectomy is required for accurate pathologic staging of gastric adenocarcinoma. *Am Surg* 2006; **72**: 849-852 [PMID: 17058719]
- Chen S,** Zhao BW, Li YF, Feng XY, Sun XW, Li W, Zhou ZW, Zhan YQ, Qian CN, Chen YB. The prognostic value of harvested lymph nodes and the metastatic lymph node ratio for gastric cancer patients: results of a study of 1,101 patients. *PLoS One* 2012; **7**: e49424 [PMID: 23166665 DOI: 10.1371/journal.pone.0049424]
- Marchet A,** Mocellin S, Ambrosi A, Morgagni P, Garcea D, Marrelli D, Roviello F, de Manzoni G, Minicozzi A, Natalini G, De Santis F, Baiocchi L, Coniglio A, Nitti D. The ratio between metastatic and examined lymph nodes (N ratio) is an independent prognostic factor in gastric cancer regardless of the type of lymphadenectomy: results from an Italian multicentric study in 1853 patients. *Ann Surg* 2007; **245**: 543-552 [PMID: 17414602 DOI: 10.1097/01.sla.0000250423.43436.e1]
- 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 [Internet]. Lyon, France: International Agency for Research on Cancer, 2013. Accessed on 3/1/2014. Available from: URL: <http://globocan.iarc.fr>
- Verlato G,** Roviello F, Marchet A, Giacomuzzi S, Marrelli D, Nitti D, de Manzoni G. Indexes of surgical quality in gastric cancer surgery: experience of an Italian network. *Ann Surg Oncol* 2009; **16**: 594-602 [PMID: 19118437 DOI: 10.1245/s10434-008-0271-x]
- Bonenkamp JJ,** Songun I, Hermans J, Sasako M, Welvaart K, Plukker JT, van Elk P, Obertop H, Gouma DJ, Taat CW. Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. *Lancet* 1995; **345**: 745-748 [PMID: 7891484 DOI: 10.1016/S0140-6736(95)90637-1]
- Cuschieri A,** Fayers P, Fielding J, Craven J, Bancewicz J, Joypaul V, Cook P. Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomised controlled surgical trial. The Surgical Cooperative Group. *Lancet* 1996; **347**: 995-999 [PMID: 8606613 DOI: 10.1016/S0140-6736(96)90144-0]
- Guadagni S,** Catarci M, de Manzoni G, Kinoshita T. D1 versus D2 dissection for gastric cancer. *Lancet* 1995; **345**: 1517; author reply 1517-1518 [PMID: 7769935 DOI: 10.1016/S0140-6736(95)91078-6]
- Fujii M,** Sasaki J, Nakajima T. State of the art in the treatment of gastric cancer: from the 71st Japanese Gastric Cancer Congress. *Gastric Cancer* 1999; **2**: 151-157 [PMID: 11957089 DOI: 10.1007/s101200050039]
- Sano T,** Sasako M, Yamamoto S, Nashimoto A, Kurita A, Hiratsuka M, Tsujinaka T, Kinoshita T, Arai K, Yamamura Y, Okajima K. Gastric cancer surgery: morbidity and mortality results from a prospective randomized controlled trial comparing D2 and extended para-aortic lymphadenectomy--Japan Clinical Oncology Group study 9501. *J Clin Oncol* 2004; **22**: 2767-2773 [PMID: 15199090 DOI: 10.1200/JCO.2004.10.184]
- Hartgrink HH,** van de Velde CJ, Putter H, Bonenkamp JJ, Klein Kranenbarg E, Songun I, Welvaart K, van Krieken JH, Meijer S, Plukker JT, van Elk PJ, Obertop H, Gouma DJ, van Lanschot JJ, Taat CW, de Graaf PW, von Meyenfeldt MF, Tilanus H, Sasako M. Extended lymph node dissection for gastric cancer: who may benefit? Final results of the randomized Dutch gastric cancer group trial. *J Clin Oncol* 2004; **22**: 2069-2077 [PMID: 15082726 DOI: 10.1200/JCO.2004.08.026]
- Wu CW,** Hsiung CA, Lo SS, Hsieh MC, Chen JH, Li AF, Lui WY, Whang-Peng J. Nodal dissection for patients

- with gastric cancer: a randomised controlled trial. *Lancet Oncol* 2006; **7**: 309-315 [PMID: 16574546 DOI: 10.1016/S1470-2045(06)70623-4]
- 24 **Wu CW**, Hsiung CA, Lo SS, Hsieh MC, Shia LT, Whang-Peng J. Randomized clinical trial of morbidity after D1 and D3 surgery for gastric cancer. *Br J Surg* 2004; **91**: 283-287 [PMID: 14991627 DOI: 10.1002/bjs.4433]
 - 25 **Nakajima T**. Gastric cancer treatment guidelines in Japan. *Gastric Cancer* 2002; **5**: 1-5 [PMID: 12021853 DOI: 10.1007/s101200200000]
 - 26 **Berrino F**, De Angelis R, Sant M, Rosso S, Bielska-Lasota M, Coebergh JW, Santaquilani M. Survival for eight major cancers and all cancers combined for European adults diagnosed in 1995-99: results of the EUROCARE-4 study. *Lancet Oncol* 2007; **8**: 773-783 [PMID: 17714991 DOI: 10.1016/S1470-2045(07)70245-0]
 - 27 **Roviello F**, Marrelli D, Morgagni P, de Manzoni G, Di Leo A, Vindigni C, Saragoni L, Tomezzoli A, Kurihara H. Survival benefit of extended D2 lymphadenectomy in gastric cancer with involvement of second level lymph nodes: a longitudinal multicenter study. *Ann Surg Oncol* 2002; **9**: 894-900 [PMID: 12417512 DOI: 10.1245/ASO.2002.02.002]
 - 28 **de Manzoni G**, Verlato GE. Gastrectomy with extended lymphadenectomy for primary treatment of gastric cancer (Br J Surg 2005; **92**: 5-13). *Br J Surg* 2005; **92**: 784 [PMID: 15912487 DOI: 10.1002/bjs.5088]
 - 29 **McCulloch P**, Nita ME, Kazi H, Gama-Rodrigues JJ. WITHDRAWN: Extended versus limited lymph nodes dissection technique for adenocarcinoma of the stomach. *Cochrane Database Syst Rev* 2012; **1**: CD001964 [PMID: 22258947 DOI: 10.1002/14651858.CD001964.pub3]
 - 30 **Vichinsky EP**, MacKlin EA, Wayne JS, Lorey F, Olivieri NF. Changes in the epidemiology of thalassemia in North America: a new minority disease. *Pediatrics* 2005; **116**: e818-e825 [PMID: 16291734 DOI: 10.1542/peds.2005-0843]
 - 31 International Comparative Performance of the UK Research Base - 2013. A report prepared by Elsevier for the UK's Department of Business, Innovation and Skills (BIS). Available from: URL: http://www.gov.uk/government/uploads/system/uploads/attachment_data/file/263729/bis-13-1297-international-comparative-performance-of-the-UK-research-base-2013.pdf
 - 32 **McCulloch P**, Taylor I, Sasako M, Lovett B, Griffin D. Randomised trials in surgery: problems and possible solutions. *BMJ* 2002; **324**: 1448-1451 [PMID: 12065273 DOI: 10.1136/bmj.324.7351.1448]
 - 33 **Japanese Gastric Cancer Association**. Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gastric Cancer* 2011; **14**: 113-123 [PMID: 21573742 DOI: 10.1007/s10120-011-0042-4]
 - 34 **Moenig S**, Baldus S, Bollschweiler E, Hoelscher A. Surgery of gastric cancer—quality assurance. *Viszeralchirurgie* 2005; **42**: 42-48
 - 35 **Meyer HJ**, Hölscher AH, Lordick F, Messmann H, Mönig S, Schumacher C, Stahl M, Wilke H, Möhler M. [Current S3 guidelines on surgical treatment of gastric carcinoma]. *Chirurg* 2012; **83**: 31-37 [PMID: 22127381 DOI: 10.1007/s00104-011-2149-x]
 - 36 **Allum WH**, Blazeby JM, Griffin SM, Cunningham D, Jankowski JA, Wong R; Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland, the British Society of Gastroenterology and the British Association of Surgical Oncology. Guidelines for the management of oesophageal and gastric cancer. *Gut* 2011; **60**: 1449-1472 [PMID: 21705456 DOI: 10.1136/gut.2010.228254]
 - 37 **Okines A**, Verheij M, Allum W, Cunningham D, Cervantes A. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2010; **21** Suppl 5: v50-v54 [PMID: 20555102 DOI: 10.1093/annonc/mdq164]
 - 38 **Waddell T**, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D. Gastric cancer: ESMO-ESSO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2013; **24** Suppl 6: vi57-vi63 [PMID: 24078663 DOI: 10.1093/annonc/mdt344]
 - 39 **Ajani JA**, Bentrem DJ, Besh S, D'Amico TA, Das P, Denlinger C, Fakih MG, Fuchs CS, Gerdes H, Glasgow RE, Hayman JA, Hofstetter WL, Ilson DH, Keswani RN, Kleinberg LR, Korn WM, Lockhart AC, Meredith K, Mulcahy MF, Orringer MB, Posey JA, Sasson AR, Scott WJ, Strong VE, Varghese TK, Warren G, Washington MK, Willett C, Wright CD, McMillian NR, Sundar H. Gastric cancer, version 2.2013: featured updates to the NCCN Guidelines. *J Natl Compr Canc Netw* 2013; **11**: 531-546 [PMID: 23667204]
 - 40 **Catalano V**, Labianca R, Beretta GD, Gatta G, de Braud F, Van Cutsem E. Gastric cancer. *Crit Rev Oncol Hematol* 2009; **71**: 127-164 [PMID: 19230702 DOI: 10.1016/j.critrevonc.2009.01.004]
 - 41 **Coburn NG**. Lymph nodes and gastric cancer. *J Surg Oncol* 2009; **99**: 199-206 [PMID: 19142901 DOI: 10.1002/jso.21224]
 - 42 **D'souza MA**, Singh K, Shrikhande SV. Surgery for gastric cancer: an evidence-based perspective. *J Cancer Res Ther* 2009; **5**: 225-231 [PMID: 20160354 DOI: 10.4103/0973-1482.59891]
 - 43 **Songun I**, van de Velde CJ. Optimal surgery for advanced gastric cancer. *Expert Rev Anticancer Ther* 2009; **9**: 1849-1858 [PMID: 19954295 DOI: 10.1586/era.09.132]
 - 44 **Yoon SS**, Yang HK. Lymphadenectomy for gastric adenocarcinoma: should west meet east? *Oncologist* 2009; **14**: 871-882 [PMID: 19738001 DOI: 10.1634/theoncologist.2009-0070]
 - 45 **Coburn NG**. Improving survival for gastric cancer patients--the role of the surgeon. *J Surg Oncol* 2010; **101**: 103-104 [PMID: 19937986 DOI: 10.1002/jso.21437]
 - 46 **de Bree E**, Charalampakis V, Melissas J, Tsiftsis DD. The extent of lymph node dissection for gastric cancer: a critical appraisal. *J Surg Oncol* 2010; **102**: 552-562 [PMID: 20976727 DOI: 10.1002/jso.21646]
 - 47 **Degiuli M**, Sasako M, Ponti A. Morbidity and mortality in the Italian Gastric Cancer Study Group randomized clinical trial of D1 versus D2 resection for gastric cancer. *Br J Surg* 2010; **97**: 643-649 [PMID: 20186890 DOI: 10.1002/bjs.6936]
 - 48 **Tanizawa Y**, Terashima M. Lymph node dissection in the resection of gastric cancer: review of existing evidence. *Gastric Cancer* 2010; **13**: 137-148 [PMID: 20820982 DOI: 10.1007/s10120-010-0560-5]
 - 49 **Maduekwe UN**, Yoon SS. An evidence-based review of the surgical treatment of gastric adenocarcinoma. *J Gastrointest Surg* 2011; **15**: 730-741 [PMID: 21399886 DOI: 10.1007/s11605-011-1477-y]
 - 50 **Doglietto GB**, Rosa F, Bossola M, Pacelli F. Lymphadenectomy for gastric cancer: still a matter of debate? *Ann Ital Chir* 2012; **83**: 199-207 [PMID: 22595731]
 - 51 **Hundahl SA**. Surgery for gastric cancer: what the trials indicate. *Surg Oncol Clin N Am* 2012; **21**: 79-97 [PMID: 22098833 DOI: 10.1016/j.soc.2011.09.005]
 - 52 **Vallbohmer D**, Oh DS, Peters JH. The role of lymphadenectomy in the surgical treatment of esophageal and gastric cancer. *Curr Probl Surg* 2012; **49**: 471-515 [PMID: 22793506 DOI: 10.1067/j.cpsurg.2012.04.003]
 - 53 **Lustosa SA**, Saconato H, Atallah AN, Lopes Filho Gde J, Matos D. Impact of extended lymphadenectomy on morbidity, mortality, recurrence and 5-year survival after gastrectomy for cancer. Meta-analysis of randomized clinical trials. *Acta Cir Bras* 2008; **23**: 520-530 [PMID: 19030751 DOI: 10.1590/S0102-86502008000600009]
 - 54 **Van Cutsem E**, Van de Velde C, Roth A, Lordick F, Köhne CH, Cascinu S, Aapro M. Expert opinion on management of gastric and gastro-oesophageal junction adenocarcinoma on behalf of the European Organisation for Research and Treatment of Cancer (EORTC)-gastrointestinal cancer group. *Eur J Cancer* 2008; **44**: 182-194 [PMID: 18093827 DOI: 10.1016/j.ejca.2007.11.001]
 - 55 **Yang SH**, Zhang YC, Yang KH, Li YP, He XD, Tian JH,

- Lv TH, Hui YH, Sharma N. An evidence-based medicine review of lymphadenectomy extent for gastric cancer. *Am J Surg* 2009; **197**: 246-251 [PMID: 18722583 DOI: 10.1016/j.amjsurg.2008.05.001]
- 56 **Memon MA**, Subramanya MS, Khan S, Hossain MB, Osland E, Memon B. Meta-analysis of D1 versus D2 gastrectomy for gastric adenocarcinoma. *Ann Surg* 2011; **253**: 900-911 [PMID: 21394009 DOI: 10.1097/SLA.0b013e318212bfff]
- 57 **Wong J**, Jackson P. Gastric cancer surgery: an American perspective on the current options and standards. *Curr Treat Options Oncol* 2011; **12**: 72-84 [PMID: 21274666 DOI: 10.1007/s11864-010-0136-y]
- 58 **Ozmen MM**, Ozmen F, Zulfikaroglu B. Lymph nodes in gastric cancer. *J Surg Oncol* 2008; **98**: 476-481 [PMID: 18720367 DOI: 10.1002/jso.21134]
- 59 **Díaz de Líaño A**, Yáñez C, Artieda C, Aguilar R, Viana S, Artajona A, Ortiz H. Results of R0 surgery with D2 lymphadenectomy for the treatment of localised gastric cancer. *Clin Transl Oncol* 2009; **11**: 178-182 [PMID: 19293056 DOI: 10.1007/S12094-009-0335-9]
- 60 **Griniatsos J**, Gakiopoulou H, Yiannakopoulou E, Dimitriou N, Douridas G, Nonni A, Liakakos T, Felekouras E. Routine modified D2 lymphadenectomy performance in pT1-T2N0 gastric cancer. *World J Gastroenterol* 2009; **15**: 5568-5572 [PMID: 19938196 DOI: 10.3748/wjg.15.5568]
- 61 **Kodera E**, Fujiwara M, Ito Y, Ohashi N, Nakayama G, Koike M, Nakao A. Radical surgery for gastric carcinoma: it is not an issue of whether to perform D1 or D2. Dissect as many lymph nodes as possible and you will be rewarded. *Acta Chir Belg* 2009; **109**: 27-35 [PMID: 19341192]
- 62 **Roy MK**, Sadhu S, Dubey SK. Advances in the management of gastric cancer. *Indian J Surg* 2009; **71**: 342-349 [PMID: 23133189 DOI: 10.1007/s12262-009-0092-6]
- 63 **Sasako M**, Inoue M, Lin JT, Khor C, Yang HK, Ohtsu A. Gastric Cancer Working Group report. *Jpn J Clin Oncol* 2010; **40** Suppl 1: i28-i37 [PMID: 20870917 DOI: 10.1093/jjco/hyq124]
- 64 **Shi Y**, Zhou Y. The role of surgery in the treatment of gastric cancer. *J Surg Oncol* 2010; **101**: 687-692 [PMID: 20512944 DOI: 10.1002/jso.21455]
- 65 **Songun I**, Putter H, Kranenbarg EM, Sasako M, van de Velde CJ. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. *Lancet Oncol* 2010; **11**: 439-449 [PMID: 20409751 DOI: 10.1016/S1470-2045(10)70070-X]
- 66 **Tentes AA**, Korakianitis O, Kyziridis D, Veliovits D. Long-term results following potentially curative gastrectomy for gastric cancer. *J BUON* 2010; **15**: 504-508 [PMID: 20941818]
- 67 **Hussain A**. Gastric malignancy: surgical management. *Curr Opin Gastroenterol* 2011; **27**: 583-587 [PMID: 21993372 DOI: 10.1097/MOG.0b013e32834a6d8d]
- 68 **Meyer HJ**, Wilke H. Treatment strategies in gastric cancer. *Dtsch Arztebl Int* 2011; **108**: 698-705; quiz 706 [PMID: 22114638 DOI: 10.3238/arztebl.2011.0698]
- 69 **Ott K**, Lordick F, Blank S, Büchler M. Gastric cancer: surgery in 2011. *Langenbecks Arch Surg* 2011; **396**: 743-758 [PMID: 21234760 DOI: 10.1007/s00423-010-0738-7]
- 70 **Saka M**, Morita S, Fukagawa T, Katai H. Present and future status of gastric cancer surgery. *Jpn J Clin Oncol* 2011; **41**: 307-313 [PMID: 21242182 DOI: 10.1093/jjco/hyq240]
- 71 **Lee JH**, Kim KM, Cheong JH, Noh SH. Current management and future strategies of gastric cancer. *Yonsei Med J* 2012; **53**: 248-257 [PMID: 22318810 DOI: 10.3349/ymj.2012.53.2.248]
- 72 **Sasako M**. Gastric cancer eastern experience. *Surg Oncol Clin N Am* 2012; **21**: 71-77 [PMID: 22098832 DOI: 10.1016/j.soc.2011.09.013]
- 73 **Seevaratnam R**, Bocicariu A, Cardoso R, Mahar A, Kiss A, Helyer L, Law C, Coburn N. A meta-analysis of D1 versus D2 lymph node dissection. *Gastric Cancer* 2012; **15** Suppl 1: S60-S69 [PMID: 22138927 DOI: 10.1007/s10120-011-0110-9]
- 74 **Viudez-Berral A**, Miranda-Murua C, Arias-de-la-Vega F, Hernández-García I, Artajona-Rosino A, Díaz-de-Liaño Á, Vera-García R. Current management of gastric cancer. *Rev Esp Enferm Dig* 2012; **104**: 134-141 [PMID: 22449155]
- 75 **Yalcin S**. Gastric cancer in Turkey-a bridge between west and East. *Gastrointest Cancer Res* 2009; **3**: 29-32 [PMID: 19343135]
- 76 **Methasate A**, Trakarnsanga A, Akaraviputh T, Chinsawangathanakol V, Lohsiriwat D. Lymph node metastasis in gastric cancer: result of D2 dissection. *J Med Assoc Thai* 2010; **93**: 310-317 [PMID: 20420105]
- 77 **Wang XN**, Liang H. Some problems in the surgical treatment of gastric cancer. *Chin J Cancer* 2010; **29**: 369-373 [PMID: 20346210]
- 78 **An JY**, Cheong JH, Hyung WJ, Noh SH. Recent evolution of surgical treatment for gastric cancer in Korea. *J Gastric Cancer* 2011; **11**: 1-6 [PMID: 22076195 DOI: 10.5230/jgc.2011.11.1.1]
- 79 **Tamura S**, Takeno A, Miki H. Lymph node dissection in curative gastrectomy for advanced gastric cancer. *Int J Surg Oncol* 2011; **2011**: 748745 [PMID: 22312521 DOI: 10.1155/2011/748745]
- 80 **Allum WH**. Optimal surgery for gastric cancer: is more always better? *Recent Results Cancer Res* 2012; **196**: 215-227 [PMID: 23129377 DOI: 10.1007/978-3-642-31629-6_15]
- 81 **Bittoni A**, Faloppi L, Giampieri R, Cascinu S. Selecting the best treatment for an individual patient. *Recent Results Cancer Res* 2012; **196**: 307-318 [PMID: 23129382 DOI: 10.1007/978-3-642-31629-6_20]
- 82 **Zilberstein B**, Mucerino DR, Yagi OK, Ribeiro-Junior U, Lopasso FP, Bresciani C, Jacob CE, Coimbra BG, Cecconello I. Results of D2 gastrectomy for gastric cancer: lymph node chain dissection or multiple node resection? *Arq Bras Cir Dig* 2012; **25**: 161-164 [PMID: 23411804 DOI: 10.1590/S0102-67202012000300005]
- 83 **Akagi T**, Shiraishi N, Kitano S. Lymph node metastasis of gastric cancer. *Cancers (Basel)* 2011; **3**: 2141-2159 [PMID: 24212800 DOI: 10.3390/cancers3022141]
- 84 **Rausei S**, Dionigi G, Rovera F, Boni L, Valerii C, Giavarini L, Frattini F, Dionigi R. A decade in gastric cancer curative surgery: Evidence of progress (1999-2009). *World J Gastrointest Surg* 2012; **4**: 45-54 [PMID: 22530078 DOI: 10.4240/wjgs.v4.i3.45]
- 85 **Lamb P**, Sivashanmugam T, White M, Irving M, Wayman J, Raimes S. Gastric cancer surgery--a balance of risk and radicality. *Ann R Coll Surg Engl* 2008; **90**: 235-242 [PMID: 18430340 DOI: 10.1308/003588408X261546]
- 86 **Brar S**, Law C, McLeod R, Helyer L, Swallow C, Paszat L, Seevaratnam R, Cardoso R, Dixon M, Mahar A, Lourenco LG, Yohanathan L, Bocicariu A, Bekaii-Saab T, Chau I, Church N, Coit D, Crane CH, Earle C, Mansfield P, Marcon N, Miner T, Noh SH, Porter G, Posner MC, Prachand V, Sano T, van de Velde C, Wong S, Coburn N. Defining surgical quality in gastric cancer: a RAND/UCLA appropriateness study. *J Am Coll Surg* 2013; **217**: 347-57.e1 [PMID: 23664139 DOI: 10.1016/j.jamcollsurg.2013.01.067]
- 87 **Jiang L**, Yang KH, Guan QL, Zhao P, Chen Y, Tian JH. Survival and recurrence free benefits with different lymphadenectomy for resectable gastric cancer: a meta-analysis. *J Surg Oncol* 2013; **107**: 807-814 [PMID: 23512524 DOI: 10.1002/jso.23325]
- 88 **Strong VE**, Yoon SS. Extended lymphadenectomy in gastric cancer is debatable. *World J Surg* 2013; **37**: 1773-1777 [PMID: 23649527 DOI: 10.1007/s00268-013-2070-1]
- 89 **Smith DL**, Elting LS, Learn PA, Raut CP, Mansfield PF. Factors influencing the volume-outcome relationship in gastrectomies: a population-based study. *Ann Surg Oncol* 2007; **14**: 1846-1852 [PMID: 17406947 DOI: 10.1245/s10434-007-9381-0]
- 90 **Krijnen P**, den Dulk M, Meershoek-Klein Kranenbarg E, Jansen-Landheer ML, van de Velde CJ. Improved survival after resectable non-cardia gastric cancer in The Netherlands: the importance of surgical training and quality control. *Eur J Surg Oncol* 2009; **35**: 715-720 [PMID: 19144490 DOI: 10.1016/j.ejso.2008.12.008]
- 91 **Jensen LS**, Nielsen H, Mortensen PB, Pilegaard HK, Johnsen

- SP. Enforcing centralization for gastric cancer in Denmark. *Eur J Surg Oncol* 2010; **36** Suppl 1: S50-S54 [PMID: 20598495 DOI: 10.1016/j.ejso.2010.06.025]
- 92 **de Steur WO**, Dikken JL, Hartgrink HH. Lymph node dissection in resectable advanced gastric cancer. *Dig Surg* 2013; **30**: 96-103 [PMID: 23867585 DOI: 10.1159/000350873]
- 93 **Dikken JL**, van Sandick JW, Allum WH, Johansson J, Jensen LS, Putter H, Coupland VH, Wouters MW, Lemmens VE, van de Velde CJ, van der Geest LG, Larsson HJ, Cats A, Verheij M. Differences in outcomes of oesophageal and gastric cancer surgery across Europe. *Br J Surg* 2013; **100**: 83-94 [PMID: 23180474 DOI: 10.1002/bjs.8966]

P- Reviewer: Izbicki JR, Ivanov KD, Li Y, Nunobe S
S- Editor: Qi Y **L- Editor:** A **E- Editor:** Wang CH





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



9 771007 932045



3 6>