16.8. 参加施設

参加施設の追加や登録可能施設の追跡協力施設への変更、研究責任者、コーディネーターの変更などによる内容変更は、プロトコール改訂・改正申請時に合わせて行い、それ以外の時に記載の変更は行わない。なお、最新の参加施設一覧はJCOGホームページ(http://www.jcog.jp/)で1か月に1度更新されているので、確認可能である。(2011年5月現在)

2011年4月より、胃がん外科グループから胃がんグループへ再編された。下記のJCOG胃がんグループのうち、本試験への参加施設は行頭に○印の付いた50施設である。

参加予定	医療機関名	科名(施設名)	研究責任者	ｺｰﾃﾞｨﾈｰﾀｰ	年間登録数見込み
○	函館厚生院函館五稜郭病院	外科	高金 明典	高金 明典	2
○	岩手医科大学	外科	肥田 圭介	藤原 久貴	2
○	国立病院機構仙台医療センター	外科	斉藤 俊博	手島 伸	2
○	宮城県立がんセンター	外科	藤谷 恒明	山並 秀章	4
○	山形県立中央病院	外科	福島 紀雅	野村 尚	5
○	栃木県立がんセンター	外科	稲田 高男	稲田 高男	3
○	防衛医科大学校	外科	長谷 和生	辻本 広紀	5
○	埼玉県立がんセンター	消化器外科	田中 洋一	川島 吉之	2
○	国立がん研究センター東病院	消化器外科	木下 平	木下 平	10
○	国立がん研究センター中央病院	胃外科	片井 均	深川 剛生	10
○	がん・感染症センター都立駒込病院	外科	岩崎 善毅	大橋 学	4
○	東京医科歯科大学	消化器外科	杉原 健一	小嶋 一幸	1
○	がん研究会有明病院	消化器外科	佐野 武	比企 直樹	10
	虎の門病院	消化器科、消化器外科、臨床腫瘍科	宇田川 晴司	貝瀬 満	-
○	都立墨東病院	外科	井上 暁	井上 暁	2
○	神奈川県立病院機構神奈川県立がんセンター	消化器外科	円谷 彰	吉川 貴己	3
○	北里大学医学部	消化器内科	小泉 和三郎	樋口 勝彦	2
○	横浜市立大学附属市民総合医療センター	消化器病センター	國崎 主税	國崎 主税	5
○	新潟県立がんセンター新潟病院	外科	梨本 篤	藪崎 裕	4
○	新潟県厚生連長岡中央綜合病院	外科	河内 保之	牧野 成人	2
○	燕労災病院	外科	宮下 薫	宮下 薫	2
○	富山県立中央病院	外科	加治 正英	加治 正英	3
○	石川県立中央病院	消化器内科	土山 寿志	稲木 紀幸	2
○	岐阜大学医学部	腫瘍外科	吉田 和弘	山口 和也	2
○	岐阜市民病院	外科	大下 裕夫	山田 誠	4
○	静岡県立総合病院	消化器センター	高木 正和	高木 正和	3
○	静岡県立静岡がんセンター	胃外科	寺島 雅典	寺島 雅典	4
○	愛知県がんセンター中央病院	消化器外科	伊藤 誠二	三澤 一成	4
○	名古屋大学医学部	消化器外科1・消化器外科2	小寺 泰弘	深谷 昌秀	2
	藤田保健衛生大学	消化管外科	宇山 一朗	石田 善敬	-
○	国立病院機構京都医療センター	外科	山口 高史	畑 啓昭	2
	京都第2赤十字病院	外科	谷口 弘毅	柿原 直樹	-
○	大阪大学医学部	消化器外科	土岐 祐一郎	黒川 幸典	3
○	近畿大学医学部	外科	今本 治彦	今野 元博	2
○	大阪府立病院機構大阪府立成人病センター	消化器外科	宮代 勲	岸 健太郎	2
○	国立病院機構大阪医療センター	外科	辻仲 利政	藤谷 和正	10
○	大阪医科大学	消化器外科	谷川 允彦	野村 栄治	3
○	市立豊中病院	外科	藤田 淳也	藤田 淳也	3
○	市立堺病院	外科	古河 洋	今村 博司	8
○	関西医科大学附属枚方病院	外科	中根 恭司	井上 健太郎	3

参加予定	医療機関名	科名(施設名)	研究責任者	ｺｰﾃﾞｨﾈｰﾀｰ	年間登録数見込み
○	神戸大学医学部	消化器内科/食道胃腸外科	東 健	奥野 達哉	2
○	関西労災病院	消化器外科	田村 茂行	三木 宏文	2
○	兵庫医科大学	上部消化管外科	笹子 三津留	松本 友寛	4
○	兵庫県立がんセンター	消化器外科	西崎 朗	川崎 健太郎	2
○	市立伊丹病院	外科	平塚 正弘	平塚 正弘	2
	天理よろづ相談所病院	腹部一般外科	吉村 玄浩	浅生 義人	−
○	和歌山県立医科大学	第2外科	山上 裕機	岩橋 誠	3
○	島根大学医学部	消化器・総合外科	田中 恒夫	平原 典幸	3
○	広島市立広島市民病院	外科	二宮 基樹	丁田 泰宏	3
○	広島市立安佐市民病院	外科	平林 直樹	杉山 陽一	2
○	福山市民病院	外科	井谷 史嗣	浅海 信也	3
○	国立病院機構四国がんセンター	消化器外科・消化器内科	栗田 啓	野崎 功雄	2
○	高知医療センター	腫瘍内科	辻 晃仁	辻 晃仁	3
○	大分大学医学部附属病院	消化器外科	北野 正剛	白石 憲男	3

計 174 人(試験開始時)

16.9. JCOGプロトコール審査委員会

本プロトコールは参加施設のIRB審査への提出に先立ちJCOGプロトコール審査委員会の審査承認を得たものである。本プロトコールの審査は以下の○印の委員および審査員が担当した。

（委員の構成・所属は承認時のもの 更新なし）

最新のものはホームページ http://www.jcog.jp/basic/org/committee/protocol.html 参照）

委員長	飛内 賢正	国立がん研究センター中央病院
副委員長	山本 精一郎	国立がん研究センターがん対策情報センター
副委員長	久保田 馨	国立がん研究センター中央病院
委員	伊藤 芳紀	国立がん研究センター中央病院
	軒原 浩	国立がん研究センター中央病院
	佐治 重衡	埼玉医科大学
	吉川 貴己	神奈川県立がんセンター
	吉野 孝之	国立がん研究センター東病院
	○佐藤 豊実	筑波大学臨床医学系
	仁保 誠治	国立がん研究センター東病院
	加藤 健	国立がん研究センター中央病院
	黒川 幸典	大阪大学
	鹿間 直人	佐久総合病院
	丸山 隆志	東京女子医科大学
	山口 拓洋	東北大学病院
	山中 竹春	国立病院機構九州がんセンター
	森田 智視	横浜市立大学大学院医学研究科
	田中 司朗	京都大学医学部附属病院
	小原 泉	自治医科大学
	稙田 いずみ	東海大学医学部
	笹山 洋子	静岡県立静岡がんセンター
	○笠井 宏委	京都大学医学部附属病院
審査員	○坪佐 恭宏	静岡県立静岡がんセンター
	○山崎 健太郎	静岡県立静岡がんセンター
事務局長	中村 健一	国立がん研究センターがん対策情報センター
事務局	鈴木 竜子	国立がん研究センターがん対策情報センター

連絡先：JCOG 運営事務局 プロトコール審査委員会事務局
国立がん研究センター がん対策情報センター 臨床試験支援部
〒104-0045 東京都中央区築地 5-1-1
TEL：03-3542-2511（内線 2404）FAX：03-3542-7006
E-mail：jcogoffice@ml.jcog.jp

16.10. JCOG効果・安全性評価委員会

研究期間中は効果・安全性評価委員会による監視（有害事象報告、中間解析審査、モニタリングレポート審査、プロトコール改訂審査など）を受ける。

（委員の構成はホームページ http://www.jcog.jp/basic/org/committee/jury.html 参照。ただし、本試験を実施する研究グループの委員は、本試験の審査には直接加わらない。）

連絡先：JCOG 効果・安全性評価委員会事務局
国立がん研究センターがん対策情報センター 臨床試験支援部/JCOG 運営事務局
〒104-0045 東京都中央区築地 5-1-1
TEL：03-3542-2511（内線 2404）FAX：03-3542-7006
E-mail：jcogoffice@ml.jcog.jp

16.11. JCOG監査委員会

研究期間中は監査委員会による施設訪問監査を受ける。
（委員の構成はホームページ http://www.jcog.jp/basic/org/committee/audit.html 参照）

連絡先：JCOG 監査委員会事務局
国立がん研究センターがん対策情報センター 臨床試験支援部/JCOG 運営事務局
〒104-0045 東京都中央区築地 5-1-1
TEL：03-3542-2511（内線 2404）
FAX：03-3542-7006
E-mail：jcogoffice@ml.jcog.jp

16.12. データセンター/運営事務局

JCOG データセンター
データセンター長 福田 治彦
国立がん研究センターがん対策情報センター 臨床試験支援部
〒104-0045 東京都中央区築地 5-1-1
TEL：03-3542-3373
FAX：03-3542-3374
E-mail：jcogdata@ml.jcog.jp

JCOG 運営事務局
運営事務局長 中村 健一
国立がん研究センターがん対策情報センター 臨床試験支援部
〒104-0045 東京都中央区築地 5-1-1
TEL：03-3542-2511（内線 2404）
FAX：03-3542-7006
E-mail：jcogoffice@ml.jcog.jp

公式ホームページ http://www.jcog.jp/

研究グループ担当者

JCOG データセンター	
統計部門	福田 治彦/柴田 大朗/水澤 純基
DM 部門	村田 尚子/坂本 有加
JCOG 運営事務局	
研究支援部門	中村 健一/木村 綾/片山 宏

16.13. プロトコール作成

プロトコール作成

愛知県がんセンター中央病院	伊藤誠二

プロトコール作成支援

JCOG データセンター	
統計部門（デザイン担当）	柴田 大朗
DM 部門（CRF 作成）	加幡 晴美/甲木 博美
JCOG 運営事務局	
研究支援部門	中村 健一/木村 綾/片山 宏
研究支援部門（ＩＣ文書担当）	木村 綾

17. 研究結果の発表

主たる公表論文は英文誌に投稿する。

研究代表者または研究事務局による、研究のエンドポイントの解析結果を含まない、研究の紹介目的の学会・論文(総説)発表や、登録終了後の、患者背景の分布や安全性データの学会・論文発表は研究グループ代表者及び JCOG データセンター長の了承を得て行うことができる。これらに該当しない、主たる解析と最終解析以外の発表については、事前に効果・安全性評価委員会の承認を得た場合を除いて行わない。

原則として、研究結果の主たる公表論文の著者は筆頭を研究事務局とし、以下、研究代表者、データセンターの統計担当(公表のための解析を行った時点での担当者 1 名)、薬物療法研究事務局、グループ代表者の順とする。それ以下は、論文の投稿規定による制限に従って、登録数の多い順に施設研究責任者または施設コーディネーターを施設毎に選び共著者とする。

すべての共著者は投稿前に論文内容を review し、発表内容に合意した者のみとする。内容に関して、議論にても合意が得られない場合、研究代表者はグループ代表者の了承の上で、その研究者を共著者に含めないことができる。

学会発表は複数回に及ぶ可能性があるため、研究事務局、研究代表者、登録の多い施設の研究責任者または施設コーディネーターの中から、持ち回りで発表を行うこととする。発表者は研究代表者がグループ代表者の了承を得て決定する。ただし、学会発表に際しては、発表準備及び発表内容について研究事務局が責任を持ち、原則としてデータセンターとの連絡は研究事務局が行う。研究事務局以外の発表者が、研究事務局と JCOG データセンター長の了承なく、直接データセンターから集計・解析結果を受け取ることはできない。

18. 付表Appendix

- 説明文書・同意書
- 体表面積表
- 毒性規準(CTCAE v4.0)
- Clavien-Dindo 手術合併症分類(JCOG 胃がん外科グループ版)
- CRF 一式

19. 参考文献

[1] 厚生労働省 人口動態調査: http://www.mhlw.go.jp/toukei/list/81-1.html

[2]独立行政法人国立がん研究センターがん対策情報センター がん情報サービス
http://ganjoho.ncc.go.jp/professional/statistics/

[3] GLOBOCAN http://globocan.iarc.fr/

[4] 日本胃癌学会. 胃癌取扱い規約 第14版: 金原出版; 2010.

[5] 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(2):51-66.

[6] 日本胃癌学会. 胃癌取扱い規約 第13版: 金原出版; 1999.

[7] 日本胃癌学会. 胃癌治療ガイドライン 第2版: 金原出版; 2004

[8] 日本胃癌学会. 胃癌治療ガイドライン 第3版: 金原出版; 2010

[9] Wanabo HJ, Kennedy BJ, Chmie CR et al.: Cancer of the stomach. A patient care study by the American College of Surgeons. Ann Surg 1993; 218: 583-592

[10] Nashimoto A, Nakajima T, Furukawa H, et al: Randomized trial of adjuvant chemotherapy with MFC followed by oral fluorouracil in serosa negative gastric cancer: JCOG Study 9206-1. J Clin Oncol 2003; 21: 2282-87.

[11] Miyashiro, H. Furukawa, M. Sasako, and K. Arai: No survival benefit with adjuvant chemotherapy for serosa-positive gastric cancer: Randomized trial of adjuvant chemotherapy with cisplatin followed by oral fluorouracil in serosa-positive gastric cancer. Japan Clinical Oncology Group 9206-2.,#4, 2005 ASCO Gastrointestinal Cancers Symposium

[12] Maehra Y, Morigucgi S, Sakaguchi Y et al.: Adjuvant chemotherapy enhances long-term survival of patients with advanced gastric cancer following curative resection. J Surg Oncol 1990; 45: 169-172

[13] Maruyama K. The Most Important Prognostic Factors for Gastric Cancer Patients: A Study Using Univariate and Multivariate Analyses. Scand.J.Gastroenterol 1987;22(S133):63-68.

[14] 岡島一雄. 胃癌患者の予後因子ー多変量解析による検討ー. 日消外会誌 1997;30:700-711.

[15] 中島聰總、太田恵一朗、大山繁和:スキルス胃癌の長期生存例. 曽根融生、井藤久雄編、スキルス胃癌ー基礎と臨床ー. 大阪、医薬ジャーナル社、1997,pp199-207

[16] 米村豊、藤村隆、伏田幸夫、他:スキルス胃癌の転移再発形式. 曽根融生、井藤久雄編、スキルス胃癌ー基礎と臨床ー. 大阪、医薬ジャーナル社、1997,pp78-98

[17] Lavonius MI, Gullichsen R, Salo S, Sonninen P, Ovaska J. Staging of gastric cancer: a study with spiral computed tomography, ultrasonography, laparoscopy, and laparoscopic ultrasonography. Surg Laparosc Endosc Percutan Tech 2002;12(2):77-81.

[18] Shimizu H, Imamura H, Ohta K, Miyazaki Y, Kishimoto T, Fukunaga M, Ohzato H, Tatsuta M, Furukawa H. Usefulness of staging laparoscopy for advanced gastric cancer. Surg Today 2010;40(2):119-24.

[19] Boku N, Ohtsu A, Shimada Y, Shirao K, Seki S, Saito H, Sakata Y, Hyodo I. Phase II study of a combination of irinotecan and cisplatin against metastatic gastric cancer. J Clin Oncol 1999;17(1):319-23.

[20] Boku N, Yamamoto S, Shirao K, Doi T, Sawaki A, Koizumi W, Saito H, Yamaguchi K, Kimura A, Ohtsu A. Randomized phase III study of 5-fluorouracil (5-FU) alone versus combination of irinotecan and cisplatin (CP) versus S-1 alone in advanced gastric cancer (JCOG9912). Presented at the 2007 ASCO Annual Meeting, Chicago, IL, June 2-5, 2007. Abstract 2007.

[21] Tsuburaya A, Sasako M, Furukawa H, Fukushima N, Fujitani T, Tanemura H, Yamamoto S. Preoperative adjuvant chemotherapy with irinotecan and cisplatin for gastric cancer with extensive lymph node metastasis: A multicenter phase II study by Japan Clinical Oncology Group (JCOG0001). Presented at the 2005 Gastrointestinal Cancers Symposium, Hollywood, Fl, January 27-29. Abstract 2005.

[22] Ando Y, Saka H, Ando M, Sawa T, Muro K, Ueoka H, Yokoyama A, Saitoh S, Shimokata K, Hasegawa Y. Polymorphisms of UDP-glucuronosyltransferase gene and irinotecan toxicity: a pharmacogenetic analysis. Cancer Res 2000;60(24):6921-6.

[23] Yoshikawa T, Sasako M, Yamamoto S, Sano T, Imamura H, Fujitani K, Oshita H, Ito S, Kawashima Y, Fukushima N. Phase II study of neoadjuvant chemotherapy and extended surgery for locally advanced gastric cancer. British Journal of Surgery 2009;96(9):1015-1022.

[24] Kawashima Y, Sasako M, Tsuburaya A, Sano T, Tanaka Y, Nashimoto A, Fukushima N, Iwasaki Y, Yamamoto S, Fukuda H. Phase II study of preoperative neoadjuvant chemotherapy (CX) with S-1 plus cisplatin for gastric cancer (GC) with bulky and/or para-aortic lymph node metastases: A Japan Clinical Oncology Group Study (JCOG0405). Presented at the 2008 Gastrointestinal Cancers Symposium, Orland, Fl, January 25-27. Abstract 2008.

[25] Koizumi W, Tanabe S, Saigenji K, Ohtsu A, Boku N, Nagashima F, Shirao K, Matsumura Y, Gotoh M. Phase I/II study of

S-1 combined with cisplatin in patients with advanced gastric cancer. Br J Cancer 2003;89(12):2207-12.
[26] Iwasaki Y, Sasako M, Sano T, Yamamoto S, Sato A, Tsujinaka T, Fukushima N, Nashimoto A, Arai K, Kinoshita T. Phase II study of preoperative S-1 and cisplatin in patients with clinically resectable type 4 and large type 3 gastric cancer: Japan Clinical Oncology Group Study (JCOG 0210). Presented at the 2006 Gastrointestinal Cancers Symposium, San Francisco, CA, January 26-28, 2006. Abstract 2006.
[27] Koizumi W, Narahara H, Hara T, Takagane A, Akiya T, Takagi M, Miyashita K, Nishizaki T, Kobayashi O, Takiyama W, Toh Y, Nagaie T, Takagi S, Yamamura Y, Yanaoka K, Orita H, Takeuchi M. S-1 plus cisplatin versus S-1 alone for first-line treatment of advanced gastric cancer (SPIRITS trial): a phase III trial. Lancet Oncol 2008;9(3):215-21.
[28] 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(5):453-62.
[29] Sakuramoto S, Sasako M, Yamaguchi T, et al. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. N Engl J Med 2007; 357: 1810-20
[30] Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, Haller DG, Ajani JA, Gunderson LL, Jessup JM, Martenson JA. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001;345(10):725-30.
[31] Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, Scarffe JH, Lofts FJ, Falk SJ, Iveson TJ, Smith DB, Langley RE, Verma M, Weeden S, Chua YJ, Participants MT. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355(1):11-20.
[32] Ajani JA, Rodriguez W, Bodoky G, Moiseyenko V, Lichinitser M, Gorbunova V, Vynnychenko I, Garin A, Lang I, Falcon S. Multicenter phase III comparison of cisplatin/S-1 with cisplatin/infusional fluorouracil in advanced gastric or gastroesophageal adenocarcinoma study: the FLAGS trial. J Clin Oncol 2010;28(9):1547-53.
[33] Taguchi T, Sakata Y, Kanamaru R, Kurihara M, Suminaga M, Ota J, Hirabayashi N. [Late phase II clinical study of RP56976 (docetaxel) in patients with advanced/recurrent gastric cancer: a Japanese Cooperative Study Group trial (group A)]. Gan To Kagaku Ryoho 1998;25(12):1915-24.
[34] Mai M, Sakata Y, Kanamaru R, Kurihara M, Suminaga M, Ota J, Hirabayashi N, Taguchi T, Furue H. [A late phase II clinical study of RP56976 (docetaxel) in patients with advanced or recurrent gastric cancer: a cooperative study group trial (group B)]. Gan To Kagaku Ryoho 1999;26(4):487-96.
[35] Ohtsu A, Shimada Y, Yoshida S, Saito H, Seki S, Morise K, Kurihara M. Phase II study of protracted infusional 5-fluorouracil combined with cisplatinum for advanced gastric cancer: report from the Japan Clinical Oncology Group (JCOG). Eur J Cancer 1994;30A(14):2091-3
[36] Sugimachi K, Maehara Y, Horikoshi N, Shimada Y, Sakata Y, Mitachi Y, Taguchi T. An early phase II study of oral S-1, a newly developed 5-fluorouracil derivative for advanced and recurrent gastrointestinal cancers. The S-1 Gastrointestinal Cancer Study Group. Oncology 1999;57(3):202-10.
[37] Yonemura Y, Sawa T, Kinoshita K, et al: Neoadjuvant chemotherapy for high grade advanced gastric cancer. World J Surg 1993; 17: 256-262
[38] Nakajima T, Ohta K, Ishihara S, et al: Combined intensive chemotherapy and radical surgery for incurative gastric cancer. Ann Surg Oncol 1997; 4:203-208
[39] Van Cutsem E, Moiseyenko VM, Tjulandin S, Majlis A, Constenla M, Boni C, Rodrigues A, Fodor M, Chao Y, Voznyi E, Risse ML, Ajani JA. Phase III study of docetaxel and cisplatin plus fluorouracil compared with cisplatin and fluorouracil as first-line therapy for advanced gastric cancer: a report of the V325 Study Group. J Clin Oncol 2006;24(31):4991-7.
[40] Sato Y, Takayama T, Sagawa T, Takahashi Y, Ohnuma H, Okubo S, Shintani N, Tanaka S, Kida M, Sato Y, Ohta H, Miyaishi K, Sato T, Takimoto R, Kobune M, Yamaguchi K, Hirata K, Niitsu Y, Kato J. Phase II study of S-1, docetaxel and cisplatin combination chemotherapy in patients with unresectable metastatic gastric cancer. Cancer Chemother Pharmacol 2010;66(4):721-8.
[41] Fushida S, Fujimura T, Oyama K, Yagi Y, Kinoshita J, Ohta T. Feasibility and efficacy of preoperative chemotherapy with docetaxel, cisplatin and S-1 in gastric cancer patients with para-aortic lymph node metastases. Anticancer Drugs 2009;20(8):752-6.
[42] Nakayama N, Koizumi W, Sasaki T, Higuchi K, Tanabe S, Nishimura K, Katada C, Nakatani K, Takagi S, Saigenji K. A multicenter, phase I dose-escalating study of docetaxel, cisplatin and S-1 for advanced gastric cancer (KDOG0601). Oncology 2008;75(1-2):1-7.
[43] Nakayama N, Koizumi W, Sasaki T, et al: Phase II study of combination therapy with docetaxel, cisplatin, and S-1 (DCS) for advanced gastric cancer: (KDOG 0601) #4555, 2009 ASCO Annual Meeting
[44] Sasako M, Mcculloch P, Kinoshita T, Maruyama K. New method to evaluate the therapeutic value of lymph node

dissection for gastric cancer.
[45] Kurokawa Y, Sasako M, Ando N, Sano T, Igaki H, Iwasaki Y, Tusuraya A, Fukuda H. Validity of response criteria in neoadjuvant chemotherapy against gastric and esophageal cancer: Correlative analyses of multicenter JCOG trials. Presented at the 2009 Gastrointestinal Cancers Symposium, Orland, Fl, January 15–17, 2009. Abstract 2009.
[46] 制吐剤適正使用ガイドライン第 1 版 金原出版、東京、2010.
[47] Journal of the National Cancer Institute, Vol. 92, No. 3, 205–216, February 2, 2000New Guidelines to Evaluate the Response to Treatment in Solid Tumors Patrick Therasse, Susan G. Arbuck, Elizabeth A. Eisenhauer, Jantien Wanders, Richard S. Kaplan, Larry Rubinstein, Jaap Verweij, Martine Van Glabbeke, Allan T. van Oosterom, Michaele C. Christian, Steve G. Gwyther

研究成果の刊行物・別刷

Gastric Cancer (2011) 14:97–100
DOI 10.1007/s10120-011-0040-6

SPECIAL ARTICLE

New Japanese classifications and treatment guidelines for gastric cancer: revision concepts and major revised points

Takeshi Sano · Takashi Aiko

Published online: 15 May 2011

1 Introduction

In 2010, the Japanese Gastric Cancer Association (JGCA) published new versions of both the Japanese Classification of Gastric Carcinoma (JC) and the Japanese Gastric Cancer Treatment Guidelines (JGL). This was the first integrated revision of the two systems, implementing major structural changes in each. The primary aim of the revision is to provide clinicians and researchers worldwide with a comprehensive and updated guide to the diagnosis and treatment of gastric cancer. English editions of the two systems are now available in this journal [1, 2].

2 History of the JC and JGL

The first edition of the JC (named "General Rules for Gastric Cancer Study") was published in 1962 to standardize the surgical and pathological documentation of gastric cancer. At that time, the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC) had not yet established a staging system for gastric cancer. Since then, the JGCA (formerly the Japanese Research Society of Gastric Carcinoma) has made periodic revisions and expanded the JC into an original comprehensive guide covering all aspects of the diagnostic and therapeutic procedures for the disease, ranging from the handling of resected specimens for pathological investigation to the extent of lymphadenectomy. It has become customary in Japan to record all cases of gastric cancer in hospital databases in accordance with the JC. Three English editions of the JC were published, corresponding to the 10th, 12th, and 13th Japanese editions, in 1981, 1995, and 1998, respectively [3–5].

In 2001, the JGCA launched the first edition of the treatment guidelines apart from the JC [6]. The primary aim of the JGL was to provide general as well as specialized clinicians with knowledge on standard treatments, based on evidence where available, and consensus, so that a patient with gastric cancer could be offered such treatments anywhere in the country. Because novel treatment modalities and novel handling of clinical issues have constantly been proposed in Japan, the JGL proposed two independent lists of stage-specific treatments; a standard list and an investigational list. This concept has been gradually and widely accepted in the clinical scene and has changed the general practice in Japan. A patients' version of the JGL was also published and has been used to enhance understanding of the treatment of gastric cancer in the general public. The second edition of the JGL was published in 2004, with minor modifications.

3 Concept of the integrated revision of the JC and JGL in 2010

The time for revision of the JC and JGL coincided for the first time in 2010. On this occasion, the JGCA committees agreed with the following concepts:

For the Japanese Gastric Cancer Association.
The online version of the two main articles referred to this prefatory article can be found under doi:10.1007/s10120-011-0041-5, and doi:10.1007/s10120-011-0042-4.

T. Sano (✉)
The Cancer Institute Hospital, Tokyo, Japan
e-mail: takeshi.sano@jfcr.or.jp

T. Aiko
Kagoshima University, Kagoshima, Japan

(a) The domains to be dealt with by the JC and the JGL should be clearly separated as follows:
   - The JC provides the basic rules to describe the status of a tumor (primary and metastatic tumor, stage grouping, histology, etc.) and the evaluation of treatment outcome (response evaluation, amount of residual disease, etc.), and will not be revised for 10 years.
   - The JGL defines the treatment methods (extent of lymphadenectomy, endoscopic resection, etc.), clarifies the indications for and details of each treatment (algorithm, chemotherapy regimens, etc.), and will be revised every 2–3 years. New important evidence requiring modification of the standard therapy will be announced on the website of the JGCA.

(b) For the description of tumor status in the JC (T/N/M categories, stage grouping, etc.), definitions identical with those in the UICC/TNM 7th edition [7] are adopted so that the Japanese experience can be expressed using the international terminology.

4 Major points revised in the JC

4.1 From the Japanese traditional T/N/M to the international T/N/M

The significations of the T/N/M categories in the new JC are identical to those in the UICC/TNM 7th edition. The modification of the N category is the largest change not only in this revision but also in the whole history of the JC. Traditionally the lymph node stations in the gastric drainage area were classified into three groups (or four in some editions) depending on the anatomical position of the station in relation to the location of the primary tumor, and these numbers were also used to express the grade of nodal metastasis (N1–3) and the extent of lymphadenectomy (D1–3); e.g., cancer with metastasis to a second group node was designated as N2, and complete dissection of up to the second group nodes was defined as D2. This rule was consistent throughout the history of the JC, though details regarding classification of the nodal groups had been modified in each edition. In the new version of the JC, this nodal grouping has been abandoned, and the N-number solely signifies the grade of nodal metastasis in terms of the number of metastatic lymph nodes as determined in the UICC/TNM 7th edition. Naturally, the extent of lymphadenectomy had to be newly defined independently from the N-category in the new JGL.

Until the current revision of the JC, the JGCA designated hepatic and peritoneal metastases as H1 and P1 and treated them separately from other distant metastasis (M1). Thus, some cases had been recorded as T3N2*M0*H1P1. In the new version, the M-category is equivalent to that of the UICC/TNM 7th edition and includes all distant metastasis. The designations of "H" and "P", however, are clinically useful and thus remain in the new JC as a subclass of the M-category.

4.2 Stage

The same stage grouping as that in the UICC/TNM 7th edition has been adopted in the new JC. It should be noted that survival analyses of a large number of the Japanese and Korean patients contributed to the determination of this UICC/TNM stage grouping [8].

4.3 Definition of the esophagogastric junction (EGJ) area

Although the JC basically complied with the staging system proposed in the UICC/TNM 7th edition, the JGCA Committee firmly denied the new UICC/TNM definition of EGJ tumors. We remain more comfortable to consider adenocarcinomas of the subcardia (Siewert type 3) as gastric cancer and believe that these should be classified and staged using the gastric scheme; not the esophageal scheme as in the UICC/TNM 7th edition. In the new JC, we adopted the definition of the EGJ area proposed by the Japan Esophageal Society [9], i.e., the area extending 2 cm above to 2 cm below the EGJ.

4.4 From "four findings" to "two classifications"

In the 1998 edition of the JC [5], clinical and pathological findings were recorded in 4 separate phases as "clinical (preoperative)", "surgical", "pathological", and "final" findings. In order to comply with the UICC/TNM system, the new JC distinguishes only clinical and pathological classifications.

4.5 Adoption of international criteria of treatment evaluation

The traditional classification "Resection (Curability) A/B/C" has been abandoned and has been replaced by "R0/1/2 (residual disease)". Staging after neoadjuvant treatment is expressed with the prefix "y". These changes are in accordance with the UICC/TNM system. For the response evaluation of chemotherapy, the response evaluation criteria in solid tumors (RECIST) version 1.1 has been adopted.

4.6 Modification of the histological diagnosis of gastric biopsy ("Group Classification")

The "Group Classification" has been widely used to diagnose the specimens obtained by endoscopic biopsy in Japan. The definitions of Groups 2 and 3 have undergone significant modifications.

5 Major points revised in the JGL

5.1 Definition of and indications for lymphadenectomy (D)

The terms "D1/D2/D3" were originally defined in the JC and have been widely used worldwide to describe the extent of lymphadenectomy. Most randomized controlled trials (RCTs) of gastric cancer surgery including the Dutch, Medical Research Council (MRC), and Taipei D1/D2 trials [10–12], were conducted using the JC definitions. However, outside these clinical studies, the terms "D1–3" have not always been used with accuracy in the strict sense. It is generally and mistakenly believed outside Japan that the first group nodes are equal to the perigastric nodes and the second group nodes are those along the celiac artery and its branches, and that the dissections of these are designated as D1 and D2, respectively. However, the original definitions of N1–3 and D1–3 are far more complicated [5]: the location of the primary tumor is determined as one of five categories (various combinations of the three equal portions of the stomach), according to which each lymph node station is given a group number (1, 2, 3, or M). For example, the left paracardial lymph nodes (station No. 2) are classified as group 1 nodes for a tumor located in the upper third of the stomach, but as group 3 nodes for a middle or middle/lower tumor, and as group *M* nodes (distant metastasis) for a tumor confined to the lower third of the stomach.

As this complicated definition of the nodal groups was established based on the results of detailed efficacy analysis of each lymph node station [13], surgeons would have the best chance to cure patients if they strictly obeyed the rule of D2. However, the grouping was too complicated to be accurately understood worldwide and, in the first place, the tumor location may not have been as correctly categorized by surgeons/pathologists as the JGCA intended to.

In the new JGL, the definition of lymphadenectomy has been remarkably simplified: the lymph node stations to be dissected in D1, D1+, and D2 are defined for total and distal gastrectomy regardless of the tumor location. D3 is no longer defined, because the rationale to recommend this super-extended surgery was lost by the negative results of our own RCT [14].

Apart from the two major types of gastrectomy (total and distal), pylorus-preserving gastrectomy and proximal gastrectomy are proposed as options for early gastric cancers, for each of which D1 and D1+ (but not D2) are defined. It should be noted that the lymph nodes along the left gastric artery (No. 7), which used to be classified as N2 for tumors in any location, are now included in the D1 for any type of gastrectomy. Lymph node station No. 14v, on the other hand, has been excluded from the D2 even for distal tumors.

The JGCA recommends that non-early, potentially curable gastric cancers should be treated by D2 lymphadenectomy. D1 or D1+ should be considered as an option for T1 tumors. D1+ can be a substitute for D2 in a poor-risk patient or under circumstances where D2 cannot be safely performed.

The JGCA expects that these simplified definitions of lymphadenectomy will help specialized surgeons worldwide to standardize gastrectomy and to obtain the best surgical results.

5.2 Chemotherapy for metastatic/recurrent gastric cancer

Several RCTs of chemotherapy for metastatic/recurrent gastric cancer were recently concluded in Japan, and for the first time in the history of the JGL, the JGCA made a recommendation of a first-line regimen for metastatic/recurrent gastric cancer; namely, S-1 + cisplatin. S-1 monotherapy was recommended for those in whom the use of cisplatin was not indicated. Although S-1 + cisplatin did not show superiority over 5-fluorouracil (FU) + cisplatin in a global randomized trial conducted outside Japan (FLAGS [15]), it has been regarded as the standard regimen for Japanese patients on the basis of two Japanese RCTs, SPIRITS [16] and JCOG9912 [17]. The JGCA also made a statement that it does not recommend the first-line use of irinotecan + cisplatin and S-1 + irinotecan because these regimens did not show superiority over 5-FU monotherapy and S-1 monotherapy, respectively [17, 18].

5.3 Adjuvant therapy after curative gastrectomy

Adjuvant chemotherapy with S-1 for patients with pathological stage II or III gastric cancer (according to the JC 13th edition) following curative D2 gastrectomy showed significantly better survival (overall and relapse-free) than surgery alone in the ACTS-GC trial [19]. The JGCA made a prompt announcement of this positive result on its website when the trial was concluded, and the recommendation has been highlighted in the new JGL. Because the definitions of stages II and III have been changed in the new JC,

the JGL now shows which stages of the new JC correspond to stages II and III in the previous edition.

Although survival benefits of adjuvant chemoradiation therapy and neoadjuvant chemotherapy have been demonstrated in the United States and Europe, evidence is yet to be established in Japan, and the JGL deals with them as investigational treatments.

6 Perspective

With this major revision of the JC, the JGCA now shares the staging system of gastric cancer with the UICC and the AJCC. We expect that the vast Japanese experience regarding this disease can now be recorded and reported in the universal language. At the same time, we expect that our simplified definitions of lymphadenectomy in the revised JGL, together with the documentation system in the JC, will provide surgeons all over the world with a standard for recording their surgery and comparing the results. Although the JGL is based primarily on evidence generated from Japanese trials, the JGCA committee is continually looking for emerging evidence throughout the world to prepare for future revisions.

References

1. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer 2011. doi: 10.1007/s10120-011-0041-5.
2. Japanese Gastric Cancer Association. Japanese Gastric Cancer Treatment Guidelines 2010 (ver. 3). Gastric Cancer 2011. doi: 10.1007/s10120-011-0042-4.
3. Kajitani T, Japanese Research Society for the Study of Gastric Cancer. The general rules for gastric cancer study in surgery and pathology. Jpn J Surg. 1981;11:127–45.
4. Japanese Research Society for Gastric Cancer. Japanese classification of gastric carcinoma. 1st English edition. Tokyo: Kanehara; 1995.
5. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 2nd English edition. Gastric Cancer. 1998;1: 10–24.
6. Nakajima T. Gastric cancer treatment guidelines in Japan. Gastric Cancer. 2002;5:1–5.
7. International Union Against Cancer. In: Sobin LH, Gospodarowicz, MK, Wittekind C, editors. TNM classification of malignant tumours. 7th ed. New Jersey: Wiley-Blackwell; 2009.
8. Ahn HS, Lee HJ, Hahn S, et al. Evaluation of the seventh American Joint Committee on Cancer/International Union Against Cancer classification of gastric adenocarcinoma in comparison with the sixth classification. Cancer. 2010;116:5592–8.
9. Japan Esophageal Society. Japanese classification of esophageal cancer, tenth edition: parts II and III. Esophagus 2009;6:71–94.
10. Bonenkamp JJ, Songun I, Hermans J, et al. Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. Lancet. 1995;345:745–8.
11. Cuschieri A, Fayers P, Fielding J, et al. Post-operative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomised controlled surgical trial. Lancet. 1996;347:995–9.
12. Wu CW, Hsiung CA, Lo SS, et al. Nodal dissection for patients with gastric cancer: a randomized controlled trial. Lancet Oncol. 2006;7:309–15.
13. Sasako M, McCulloch P, Kinoshita T, Maruyama K. New method to evaluate the therapeutic value of lymph node dissection for gastric cancer. Br J Surg. 1995;82:346–51.
14. Sasako M, Sano T, Yamamoto S, et al. D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. N Engl J Med. 2008;359:453–62.
15. Ajani JA, Rodriguez W, Bodoky G, et al. Multicenter phase III comparison of cisplatin/S-1 with cisplatin/infusional fluorouracil in advanced gastric or gastroesophageal adenocarcinoma study: The FLAGS trial. J Clin Oncol. 2010;28:1547–53.
16. Koizumi W, Narahara H, Hara T, et al. Randomized phase III study of S-1 alone versus S-1 + cisplatin in the treatment for advanced gastric cancer (The SPIRITS trial): a phase III trial. Lancet Oncol. 2008;9:215–21.
17. Boku N, Yamamoto S, Shirao K, et al. Fluorouracil versus combination of irinotecan plus cisplatin versus S-1 in metastatic gastric cancer: a randomized phase 3 study. Lancet Oncol. 2009;10:1063–9.
18. Narahara H, Iishi H, Imamura H, et al. Randomized phase III study comparing the efficacy and safety of irinotecan plus S-1 with S-1 alone as first-line treatment for advanced gastric cancer (study GC0301/TOP–002). Gastric Cancer. 2011;14:72–80.
19. Sakuramoto S, Sasako M, Yamaguchi T, et al. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. N Engl J Med. 2007;357:1810–20.

Gastric Cancer (2011) 14:178–182
DOI 10.1007/s10120-011-0012-x

SHORT COMMUNICATION

General perioperative management of gastric cancer patients at high-volume centers

Hye Seong Ahn · Jeong Hwan Yook · Cho Hyun Park · Young Kyu Park · Wansik Yu · Moon-Soo Lee · Han Sang-Uk · Keun Won Ryu · Tae Sung Sohn · Hyung-Ho Kim · Seung Ho Choi · Sung Hoon Noh · Naoki Hiki · Takeshi Sano · Han-Kwang Yang

Received: 6 April 2010 / Accepted: 31 October 2010 / Published online: 5 March 2011

Abstract
Background Gastric cancer is very common in Korea and Japan, where many hospitals annually perform high numbers of gastrectomies for gastric cancer. The aim of this study was to compare the general management of gastric cancer in high-volume centers in Korea and Japan.

Methods We undertook a survey of the general management of gastric cancer at high-volume centers (over 200 cases/year) and analyzed the answers.

Results In six of 14 hospitals surveyed, antimicrobial prophylaxis for elective gastrectomy was administered until postoperative day 3. A Levin tube and an abdominal drain were routinely inserted in seven and ten hospitals, respectively. Laboratory tests, such as complete blood cell

H. S. Ahn · H.-K. Yang (✉)
Department of Surgery and Cancer Research Institute, Seoul National University College of Medicine, 28 Yeongeon-dong, Jongno-gu, Seoul 110-744, Korea
e-mail: hkyang@snu.ac.kr

J. H. Yook
Department of Surgery, Asan Medical Center, Seoul, Korea

C. H. Park
Department of Surgery, Catholic University Seoul St. Mary Hospital, Seoul, Korea

Y. K. Park
Department of Surgery, Chonnam National University Hospital, Gwangju, Korea

W. Yu
Department of Surgery, Kyungpook National University Hospital, Daegu, Korea

M.-S. Lee
Department of Surgery, Soon Chun Hyang University Cheonan Hospital, Cheonan, Korea

H. Sang-Uk
Department of Surgery, Ajou University Hospital, Suwon, Korea

K. W. Ryu
Division of Gastric Cancer, National Cancer Center, Goyang, Korea

T. S. Sohn
Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

H.-H. Kim
Department of Surgery, Seoul National University Bundang Hospital, Seongnam, Korea

S. H. Choi
Department of Surgery, Yonsei University Kangnam Severance Hospital, Seoul, Korea

S. H. Noh
Department of Surgery, Yonsei University Severance Hospital, Seoul, Korea

N. Hiki
Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan

T. Sano
National Cancer Center, Tokyo, Japan

Present Address:
T. Sano
Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan

count, liver function test, electrolytes, and blood urea nitrogen/creatinine were performed frequently on postoperative days 1, 2, 3, and 5. Sips of water after open distal gastrectomy were restarted up to postoperative day 3 in twelve hospitals. The surgical pathology was reported up to postoperative day 10 in thirteen hospitals. Twelve hospitals provided a regular patient education program and only one hospital provided an integrated education program which included the participation of a surgeon, an oncologist, a nurse, and a nutritionist.

Conclusions The general management of gastric cancer in 14 high-volume centers was not so different among the centers. The general management protocols noted here are expected to provide useful information for perioperative care.

Keywords Gastric cancer · General management · High-volume center

Introduction

Gastric cancer is the one of the most serious health problems in Korea and Japan [1, 2]. However, the overall survival rates after surgical treatment have been increasing and the rate of postoperative complications has decreased [2, 3]. Probably, these improvements are due to the introduction of more radical surgical techniques ; early detection ; and the improvement of anesthesia, perioperative care, and nutritional support. In addition, because of the high incidence of gastric cancer, many surgeons in Korea and Japan have accumulated substantial experience in the management of the disease, and have developed general protocols of perioperative management for patients with gastric cancer. However, there are several controversial issues in the general perioperative management of gastric cancer, such as Levin tube decompression, abdominal drain insertion, and antimicrobial prophylaxis. The aims of this study were to compare the general perioperative management of patients with gastric cancer in Korean and Japanese high-volume centers and to contribute to the improvement of surgical outcomes and to the development of site-specific protocols.

Methods

A brief questionnaire about the general perioperative management of patients with gastric cancer was sent in 2007, via email, to representative surgeons at Korean and Japanese high-volume centers where more than 200 operations were performed per year. In addition, two leading cancer centers in Japan were invited to participate in the surveillance. The survey form included 12 items, shown as Table 1. Each item was analyzed and compared among the institutions. For descriptive analysis, SPSS version 12.0 (SPSS, Chicago, IL, USA) was used.

Table 1 Form used for the survey of general perioperative management implemented at each high-volume center

Item	Answer
Where is preoperative workup performed?	(1) At outpatient clinic (OPD) (2) after admission
Prophylactic antibiotics	Regimen:
	Duration:
Analgesics	Regimen:
	Duration:
Levin tube	(1) Inserted (2) not inserted
	Duration:
Abdominal drainage tube	(1) Inserted (2) not inserted
For subtotal and total gastrectomy	Duration:
If different, please describe separately	
Postoperative laboratory tests	What items?
	When?
Main type of fluid infused after surgery	
Schedule for oral intake	
Schedule for discharge	
Time required to receive pathology report (days)	
EMR (electronic medical record)—based critical pathway (CP)	(1) Performed (2) not performed
Regular patient education program	Interval of education:
	Education time:
	Lecturer:

(1) If different pathways are applied on a case-by-case basis (i.e., early gastric cancer vs. advanced gastric cancer; subtotal gastrectomy vs. total gastrectomy), please duplicate the relevant question box and fill out the answers separately

(2) If some items are difficult to assess, leave the corresponding box empty

Results

The answers from representative surgeons at 14 hospitals were analyzed.

Preoperative workup was performed after admission in 3 hospitals, and most workup was done before admission in 11 hospitals.

In three hospitals (3/14), antimicrobial prophylaxis for elective gastrectomy was administered for 24 h or less; it was administered up to postoperative day 2 in five hospitals and up to postoperative day 3 in six. The most frequently administered antibiotic was a second-generation cephalosporin ($n = 8$), followed by a first-generation cephalosporin ($n = 4$) and a third-generation cephalosporin ($n = 2$). In four hospitals, a cephalosporin and an aminoglycoside were chosen for prophlyaxis.

For pain control, patients received patient-controlled anesthesia (PCA) intravenously ($n = 9$) or epidurally ($n = 5$) until postoperative day 2 or 3.

Surgeons at five hospitals (5/14) did not insert a Levin tube preoperatively. However, in seven hospitals (7/14), the tube was inserted preoperatively and removed on postoperative day 1 ($n = 5$) or just after surgery ($n = 2$). Surgeons at another two hospitals (2/14) inserted a tube only in the patients with advanced gastric cancer or obstruction.

Surgeons at two (2/14) hospitals did not insert an abdominal drain, and surgeons at two other hospitals inserted abdominal drains on a case-by-case basis. However, surgeons at ten (10/14) hospitals inserted one or two abdominal drains according to the extent of resection (total or distal gastrectomy) or according to the anastomosis method (Billroth I or Billroth II). Although the time of drain removal varied from postoperative day 2 to postoperative day 6, the most frequent postoperative days of drain removal were postoperative days 3–4 ($n = 7$).

Samples for laboratory tests were taken more than once. Usually the tests included a complete blood cell count, liver function test, electrolytes, blood urea nitrogen/creatinine, C-reactive protein, and chest X-ray. The most frequent time for laboratory tests was postoperative day 1 ($n = 8$) followed by postoperative days 2 ($n = 6$), 5 ($n = 5$), and 3 ($n = 4$).

Five or ten percent dextrose solutions were infused in six hospitals prior to the initiation of oral diet. In four hospitals, patients received peripheral total parenteral nutrition. The status of use of other fluids such as amino acids or lipids could not be compared due to the limited number of answers.

Sips of water after open distal gastrectomy were restarted on postoperative day 3 ($n = 9$) and on postoperative day 2 ($n = 3$). Surgeons at some hospitals answered that the day of oral diet resumption was different according to the surgical approach (open or laparoscopic) and the extent of resection. In 2 hospitals, patients who underwent total gastrectomy resumed oral diet later than patients who underwent subtotal gastrectomy. And surgeons at three hospitals answered that patients who underwent laparoscopic gastrectomy resumed oral diet earlier than patients who underwent open gastrectomy.

Patients who underwent subtotal gastrectomy were discharged on postoperative day 6 or 7 ($n = 7$), 8 or 9 ($n = 4$), 10 or 11($n = 2$), or 5 ($n = 1$). At three hospitals, patients who underwent total gastrectomy were discharged 1–3 days later than patients who underwent subtotal gastrectomy. And surgeons at two hospitals answered that patients who underwent laparoscopy-assisted gastrectomy were discharged 1 or 2 days earlier than patients who underwent open gastrectomy. Patients in two Japanese hospitals seemed to stay longer than patients in Korean hospitals (10.5–11 vs. 6–9 days).

Surgical pathology was reported until postoperative day 10 at thirteen hospitals. In 3 hospitals only 3–5 days after surgery was required to get these reports. Two Japanese hospitals seemed to require more time (up to 28 days) than the Korean hospitals, especially when the tumor metastasis to lymph nodes.

Six hospitals had electronic medical record-based critical pathways and the other hospitals had a printed order set. Twelve hospitals provided a regular patient education program and nine hospitals had a nutritional counseling and support system. Four hospitals had group-educational programs and the other ten hospitals seemed to have only individual programs begun when the patient restarted oral diet or was discharged. Only one hospital provided an integrated education program which included the participation of a surgeon, a medical oncologist, a nurse, and a nutritionist.

Discussion

The mortality and morbidity after surgery for many cancers other than gastric cancer are known to be influenced by the hospital patient volume [4, 5]. The existence of many high-volume centers for gastric cancer in Korea and Japan may have led to the low morbidity and mortality observed for patients after radical gastrectomy with lymphadenectomy [6, 7].

As for antimicrobial prophylaxis, according to the Centers for Disease Control (CDC) guidelines and references, a first-generation cephalosporin should be administered as antimicrobial prophylaxis in clean-contaminated operations within 30 min of the first surgical incision, with intraoperative supplemental administration every 3–4 h and postoperative administration for 24 h or less [8]. The

Health Insurance Review and Assessment Service of Korea has recommended that a first- or second-generation cephalosporin should be administered as prophylaxis in gastrointestinal surgery, and administration should be started within 30 min or 1 h of skin incision and last for 24 h or less; in addition they note that aminoglycosides are not suitable for prophylaxis because of renal toxicity and ototoxicity [9]. Although the present study showed many discrepancies between guidelines and actual practice, the risk and benefit should be balanced for the appropriate use of antimicrobial prophylaxis.

Recently several studies, albeit with limited scientific evidence levels, have reported that Levin tube decompression was not correlated with earlier recovery of bowel function, shorter hospital stay, reduced anastomotic leakage, or fewer pulmonary complications after gastrectomy for gastric cancer [10, 11]. These findings might explain why surgeons in 5 of the 14 hospitals did not insert a Levin tube. With regard to abdominal drain tubes, prophylactic drain placement has been widely practiced by gastric surgeons. Surgeons who inserted abdominal drains might believe that the prophylactic use of drains provides early information about such factors as anastomotic leakage and intraabdominal bleeding. However, these benefit of prophylactic use of drain was not proven in two studies [12, 13]. The placement of a Levin tube and an abdominal drain in operations for gastric cancer warrants further investigation through large-scale randomized clinical trials.

Although many studies have shown that early oral feeding is feasible after gastrectomy, the optimal dietary schedule has not been established [14, 15]. Traditionally, postoperative oral intake after abdominal surgery was slowly and carefully introduced, due to anstomotic leakage and postoperative paralytic ileus. Malnutrition as one symptom arising from gastric cancer or one major complication after radical gastrectomy is known to be related to the quality of life, morbidity and mortality, and survival of patients after gastrectomy [16, 17]. These factors seemed to lead many hospitals in this study to adopt a policy of early oral intake and to implement nutritional counseling programs or group-educational programs.

There was a tendency in the present study that patients who underwent laparoscopic surgery resumed oral feeding earlier and were discharged later than patients who underwent open gastrectomy, although not all participants answered that there were different protocols for patients who underwent laparoscopic gastrectomy. Although two Japanese hospitals could not be taken to represent all hospitals in Japan, patients in these two hospitals were discharged relatively later than patients in the Korean hospitals, and the surgical pathology reports in the Japanese hospitals required more time, too. This longer hospital stay is in accordance with many reports showing a mean postoperative hospital stay of 15–32 days in Japan, which is relatively much longer than that in Korean hospitals (7–13 days) [6, 18–21]. The longer hospital stay in the Japanese institutions might reflect differences in the medical insurance systems.

Conclusion

The general perioperative management of gastric cancer patients at 14 high-volume centers was not so different among the hospitals, except that the hospital stay and the time required for obtaining surgical pathology reports were relatively longer in the Japanese hospitals than in the Korean hospitals. The general perioperative management information obtained in the present study could help many gastric surgeons to establish their own protocols and to improve surgical outcomes.

References

1. Lee HJ, Yang HK, Ahn YO. Gastric cancer in Korea. Gastric Cancer. 2002;5(3):177–82.
2. Maehara Y, Kakeji Y, Oda S, Takahashi I, Akazawa K, Sugimachi K. Time trends of surgical treatment and the prognosis for Japanese patients with gastric cancer. Br J Cancer. 2000;83(8):986–91.
3. Borch K, Jonsson B, Tarpila E, Franzen T, Berglund J, Kullman E, et al. Changing pattern of histological type, location, stage and outcome of surgical treatment of gastric carcinoma. Br J Surg. 2000;87(5):618–26.
4. Begg CB, Cramer LD, Hoskins WJ, Brennan MF. Impact of hospital volume on operative mortality for major cancer surgery. JAMA. 1998;280(20):1747–51.
5. Schrag D, Cramer LD, Bach PB, Cohen AM, Warren JL, Begg CB. Influence of hospital procedure volume on outcomes following surgery for colon cancer. JAMA. 2000;284(23):3028–35.
6. Park DJ, Lee HJ, Kim HH, Yang HK, Lee KU, Choe KJ. Predictors of operative morbidity and mortality in gastric cancer surgery. Br J Surg. 2005;92(9):1099–102.
7. Kodera Y, Sasako M, Yamamoto S, Sano T, Nashimoto A, Kurita A. Identification of risk factors for the development of complications following extended and superextended lymphadenectomies for gastric cancer. Br J Surg. 2005;92(9):1103–9.
8. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Am J Infect Control. 1999;27(2):97–132.
9. http://www.hira.or.kr/common/dummy.jsp?pgmid=HIRAB03020 2010000 Accessed 20 Oct 2010.
10. Doglietto GB, Papa V, Tortorelli AP, Bossola M, Covino M, Pacelli F. Nasojejunal tube placement after total gastrectomy: a multicenter prospective randomized trial. Arch Surg 2004;139(12):1309–13; discussion 13.
11. Yang Z, Zheng Q, Wang Z. Meta-analysis of the need for nasogastric or nasojejunal decompression after gastrectomy for gastric cancer. Br J Surg. 2008;95(7):809–16.

12. Kim J, Lee J, Hyung WJ, Cheong JH, Chen J, Choi SH, et al. Gastric cancer surgery without drains: a prospective randomized trial. J Gastrointest Surg. 2004;8(6):727–32.
13. Kumar M, Yang SB, Jaiswal VK, Shah JN, Shreshtha M, Gongal R. Is prophylactic placement of drains necessary after subtotal gastrectomy? World J Gastroenterol. 2007;13(27):3738–41.
14. Heslin MJ, Latkany L, Leung D, Brooks AD, Hochwald SN, Pisters PW, et al. A prospective, randomized trial of early enteral feeding after resection of upper gastrointestinal malignancy. Ann Surg 1997;226(4):567–77; discussion 77–80.
15. Hirao M, Tsujinaka T, Takeno A, Fujitani K, Kurata M. Patient-controlled dietary schedule improves clinical outcome after gastrectomy for gastric cancer. World J Surg. 2005;29(7):853–7.
16. Bae JM, Park JW, Yang HK, Kim JP. Nutritional status of gastric cancer patients after total gastrectomy. World J Surg 1998; 22(3):254–60; discussion 60–1.
17. Sategna-Guidetti C, Bianco L. Malnutrition and malabsorption after total gastrectomy. A pathophysiologic approach. J Clin Gastroenterol. 1989;11(5):518–24.
18. Kitano S, Shiraishi N, Kakisako K, Yasuda K, Inomata M, Adachi Y. Laparoscopy-assisted Billroth-I gastrectomy (LADG) for cancer: our 10 years' experience. Surg Laparosc Endosc Percutan Tech. 2002;12(3):204–7.
19. Ishikawa M, Kitayama J, Kaizaki S, Nakayama H, Ishigami H, Fujii S, et al. Prospective randomized trial comparing Billroth I and Roux-en-Y procedures after distal gastrectomy for gastric carcinoma. World J Surg 2005;29(11):1415–20; discussion 21.
20. Adachi Y, Shiraishi N, Shiromizu A, Bandoh T, Aramaki M, Kitano S. Laparoscopy-assisted Billroth I gastrectomy compared with conventional open gastrectomy. Arch Surg. 2000; 135(7):806–10.
21. Kim MC, Kim W, Kim HH, Ryu SW, Ryu SY, Song KY, et al. Risk factors associated with complication following laparoscopy-assisted gastrectomy for gastric cancer: a large-scale Korean multicenter study. Ann Surg Oncol. 2008;15(10):2692–700.

Original article

Functional outcomes after extended surgery for gastric cancer

Y. Kurokawa[1], M. Sasako[2], T. Sano[3], T. Shibata[8], S. Ito[4], A. Nashimoto[5], A. Kurita[6] and T. Kinoshita[7], for the Japan Clinical Oncology Group

Departments of Surgery, [1]Osaka National Hospital, Osaka, [2]Hyogo College of Medicine, Nishinomiya, [3]Cancer Institute Ariake Hospital, Tokyo, [4]Aichi Cancer Centre, Nagoya, [5]Niigata Cancer Centre Hospital, Niigata, [6]National Shikoku Cancer Centre, Matsuyama, and [7]National Cancer Centre Hospital East, Kashiwa, and [8]Japan Clinical Oncology Group Data Centre, Centre for Cancer Control and Information Services, National Cancer Centre, Tokyo, Japan

Correspondence to: Dr Y. Kurokawa, Department of Gastroenterological Surgery, Osaka University Graduate School of Medicine, 2-2-E2, Yamadaoka, Suita, Osaka 565-0871, Japan (e-mail: ykurokawa@gesurg.med.osaka-u.ac.jp)

Background: Extended gastrectomy with para-aortic nodal dissection (PAND) or thorough dissection of mediastinal nodes using a left thoracoabdominal (LTA) approach is an alternative to D2 lymphadenectomy, with variable postoperative results.

Methods: Two randomized controlled trials have been conducted to compare D2 lymphadenectomy alone (263 patients) *versus* D2 lymphadenectomy plus PAND (260), and the abdominal–transhiatal (TH) approach (82) *versus* the LTA approach (85), in patients with gastric cancer. Prospectively registered secondary endpoints bodyweight, symptom scores and respiratory function were evaluated in the present study.

Results: Bodyweight was comparable after D2 and D2 plus PAND, but higher after TH than after LTA procedures at 1 and 3 years. At 1- and 3-year follow-up symptom scores were comparable between D2 and D2 plus PAND. A LTA approach resulted in significantly worse scores than a TH approach in terms of meal volume, return to work, incisional pain and dyspnoea up to 1 year. The decrease in vital capacity was significantly greater after LTA than TH procedures up to 6 months.

Conclusion: Bodyweight and postoperative symptoms were not affected by adding PAND to a D2 procedure. A LTA approach aggravated weight loss, symptoms and respiratory functions compared with a TH approach. Registration numbers: NCT00149279, NCT00149266 (http://www.clinicaltrials.gov).

Paper accepted 26 August 2010

Published online 22 November 2010 in Wiley Online Library (www.bjs.co.uk). **DOI:** 10.1002/bjs.7297

Introduction

Radical gastrectomy with D2 lymphadenectomy is the standard treatment for patients with curable gastric cancer in east Asia[1]. To improve survival further, more extensive surgery has been attempted in specialized centres. Two multicentre randomized controlled trials have evaluated extended gastric surgery. In the Japan Clinical Oncology Group (JCOG) 9501 trial, D2 plus para-aortic nodal dissection (PAND) was compared with D2 lymphadenectomy for tumour category (T) 2b to T4 potentially curable gastric cancer[2,3]. In the JCOG9502 trial, a left thoracoabdominal (LTA) approach accompanied by thorough lower mediastinal lymphadenectomy was compared with an abdominal–transhiatal (TH) approach for proximal gastric cancer invading the oesophagus[4].

Contrary to expectations, there was no survival benefit from these extended procedures. D2 plus PAND or a LTA approach resulted in a longer duration of operation than D2 or a TH procedure. The morbidity was also worse after these extended procedures than after the standard operations. This has led to the conclusion that they should not be employed as prophylactic lymphadenectomy for curable gastric cancer[2,4]. Apart from survival and short-term morbidity, postoperative evaluation of symptom, bodyweight and respiratory function outcomes after extended surgery permits proper decision-making regarding surgical treatment for gastric cancer. In the present study, changes in the secondary endpoints bodyweight, various symptom-related scores and respiratory function in these two trials were assessed prospectively.