［B 群］ 対象:2013 年 1 月 31 日までに追跡調査用紙 2 が回収された 347 例

	CTCAE4.0	G0	G1	G2	G3	G4	%G2-4	%G3-4	%G4	合計	欠損
腹腔内膿瘍	腹膜感染										
消化管 吻合部狭窄	傷害、中毒および処置合併症、その他（吻合部狭窄）										
胆嚢炎	胆嚢炎										
ダンピング症候群	胃腸障害、その他（ダンピング症候群）										
逆流性食道炎	胃食道逆流性疾患										
閉塞性イレウス	小腸閉塞										
麻痺性イレウス	イレウス										
術後肺炎	肺感染										
術後創感染	創傷感染										
腹壁瘢痕 ヘルニア	創合併症										

	Clavien-Dindo	G0	GⅠ	GⅡ	GⅢa	GⅢb	GⅣa	GⅣb	%GⅡ-Ⅳb	%GⅢa-Ⅳb	%GⅣa-Ⅳb	合計	欠損
腹腔内膿瘍	腹腔内膿瘍												
消化管 吻合部狭窄	消化管 吻合部狭窄												
胆嚢炎	胆嚢炎												
ダンピング症候群	ダンピング症候群												
逆流性食道炎	逆流性食道炎												
閉塞性イレウス	閉塞性イレウス												
麻痺性イレウス	麻痺性イレウス												
術後肺炎	術後肺炎												
術後創感染	術後創感染												
腹壁瘢痕 ヘルニア	腹壁瘢痕 ヘルニア												

胃がんグループ/参加医療機関のみ

［合計］ 対象:2013 年 1 月 31 日までに追跡調査用紙 2 が回収された 694 例

因果関係なし[not related,unlikely]を除く（因果関係なし[A:not related, B:unlikely]は、「Grade0」にカウントした）

	CTCAE4.0	G0	G1	G2	G3	G4	%G2-4	%G3-4	%G4	合計	欠損
腹腔内膿瘍	腹膜感染	690	－	－	4	0	0.6	0.6	0	694	
消化管 吻合部狭窄	傷害、中毒および処置合併症、その他（吻合部狭窄）	692	0	0	2	0	0.3	0.3	0	694	
胆嚢炎	胆嚢炎	692	－	2	0	0	0.3	0	0	694	
ダンピング症候群	胃腸障害、その他（ダンピング症候群）	655	37	2	0	0	0.3	0	0	694	
逆流性食道炎	胃食道逆流性疾患	672	17	5	0	－	0.7	0	－	694	
閉塞性イレウス	小腸閉塞	690	0	1	2	1	0.6	0.4	0.1	694	
麻痺性イレウス	イレウス	694	－	0	0	0	0	0	0	694	
術後肺炎	肺感染	692	－	2	0	0	0.3	0	0	694	
術後創感染	創傷感染	690	－	3	0	0	0.4	0	0	694	
腹壁瘢痕 ヘルニア	創合併症	690	4	0	0	0	0	0	0	694	

因果関係なし[A:not related, B:unlikely]と報告され、「Grade0」にカウントした一覧

No.	施設名	有害事象	Grade	因果関係（担当医報告）	出現時期	詳細
7	神奈川県立がんセンター	肺感染	3	B	11 年度前期	POD317 より食欲不振が続いていたが、POD324 の朝 39 度の発熱と電話があり来院された。XP と CT により発熱性好中球減少に伴う肺炎と診断され同日入院、治療し、22 日後に軽快退院 【研究事務局レビューにて】 担当医より「発熱性好中球減少に伴う肺炎」と報告があったが、定型項目の「肺感染」とした。
76	国立がん研究センター中央病院	胃腸障害、その他（ダンピング症候群）	1	B	11 年度前期	なし
121	神奈川県立がんセンター	肺感染	2	B	11 年度後期	なし

	Clavien-Dindo	G0	GⅠ	GⅡ	GⅢa	GⅢb	GⅣa	GⅣb	%GⅡ-Ⅳb	%GⅢa-Ⅳb	%GⅣa-Ⅳb	合計	欠損
腹腔内膿瘍	腹腔内膿瘍	690	0	2	1	1	0	0	0.6	0.3	0	694	
消化管 吻合部狭窄	消化管 吻合部狭窄	692	0	1	1	0	－	－	0.3	0.1	－	694	
胆嚢炎	胆嚢炎	691	1	1	0	0	0	0	0.1	0	0	693	1
ダンピング症候群	ダンピング症候群	658	33	3	－	0	－	－	0.4	0	－	694	
逆流性食道炎	逆流性食道炎	672	17	5	－	0	－	－	0.7	0	－	694	
閉塞性イレウス	閉塞性イレウス	690	0	1	0	3	0	0	0.6	0.4	0	694	
麻痺性イレウス	麻痺性イレウス	694	0	0	0	0	0	0	0	0	0	694	
術後肺炎	術後肺炎	691	1	2	0	0	0	0	0.3	0	0	694	
術後創感染	術後創感染	690	1	3	0	0	0	0	0.4	0	0	694	
腹壁瘢痕 ヘルニア	腹壁瘢痕 ヘルニア	690	4	0	0	0	0	0	0	0	0	694	

因果関係なし[A:not related, B:unlikely]と報告され、「Grade0」にカウントした一覧

No.	施設名	有害事象	Grade	因果関係（担当医報告）	出現時期	詳細
76	国立がん研究センター中央病院	胃腸障害、その他（ダンピング症候群）	Ⅰ	B	11 年度後期	なし

胃がんグループ/参加医療機関のみ

No.	施設名	有害事象	Grade	因果関係 (担当医報告)	出現時期	詳細
86	国立がんセンター 中央病院	肺感染	I	A	11 年度前期	なし
121	神奈川県立がん センター	肺感染	II	B	11 年度後期	なし

[合計] 対象:2013 年 1 月 31 日までに追跡調査用紙 2 が回収された 694 例
因果関係なし[A:not related, B:unlikely]を含む

	CTCAE4.0	G0	G1	G2	G3	G4	%G2-4	%G3-4	%G4	合計	欠損
腹腔内膿瘍	腹膜感染	690	—	—	4	0	0.6	0.6	0	694	
消化管 吻合部狭窄	傷害、中毒および 処置合併症、その他 (吻合部狭窄)	692	0	0	2	0	0.3	0.3	0	694	
胆嚢炎	胆嚢炎	692	—	2	0	0	0.3	0	0	694	
ダンピング症候群	胃腸障害、その他 (ダンピング症候群)	655	37	2	0	0	0.3	0	0	694	
逆流性食道炎	胃食道逆流性疾患	672	17	5	0	—	0.7	0	—	694	
閉塞性イレウス	小腸閉塞	690	0	1	2	1	0.6	0.4	0.1	694	
麻痺性イレウス	イレウス	694	—	0	0	0	0	0	0	694	
術後肺炎	肺感染	690	—	3	1	0	0.6	0.1	0	694	
術後創感染	創傷感染	690	—	3	0	0	0.4	0	0	694	
腹壁瘢痕 ヘルニア	創合併症	690	4	0	0	0	0	0	0	694	

	Clavien-Dindo	G0	G I	G II	G IIIa	G IIIb	G IVa	G IVb	%G II -IVb	%G III a-IVb	%G IV a-IVb	合計	欠損
腹腔内膿瘍	腹腔内膿瘍	690	0	2	1	1	0	0	0.6	0.3	0	694	
消化管 吻合部狭窄	消化管 吻合部狭窄	692	0	1	1	0	—	—	0.3	0.1	—	694	
胆嚢炎	胆嚢炎	691	1	1	0	0	0	0	0.1	0	0	693	1
ダンピング症候群	ダンピング症候群	658	33	3	—	0	—	—	0.4	0	—	694	
逆流性食道炎	逆流性食道炎	672	17	5	—	0	—	—	0.7	0	—	694	
閉塞性イレウス	閉塞性イレウス	690	0	1	0	3	0	0	0.6	0.4	0	694	
麻痺性イレウス	麻痺性イレウス	694	0	0	0	0	0	0	0	0	0	694	
術後肺炎	術後肺炎	689	2	3	0	0	0	0	0.4	0	0	694	
術後創感染	術後創感染	690	1	3	0	0	0	0	0.4	0	0	694	
腹壁瘢痕 ヘルニア	腹壁瘢痕 ヘルニア	690	4	0	0	0	0	0	0	0	0	694	

8. 有効性の評価

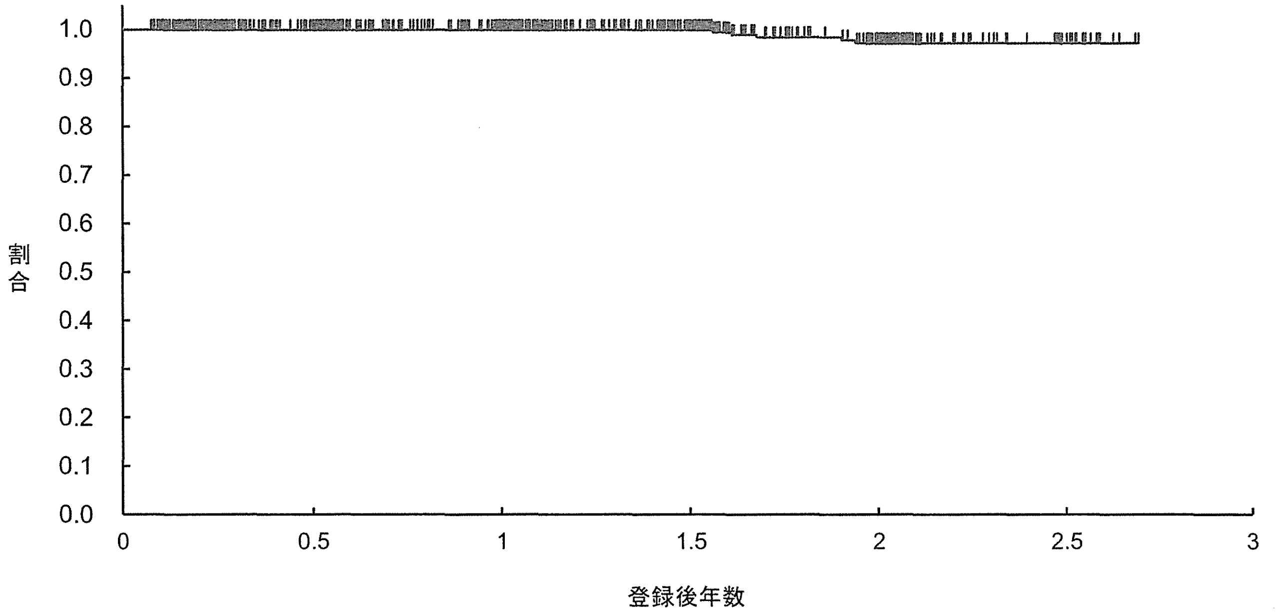
「1 年 = 365.25 日」「1 か月 =(365.25/12)日」で計算

全生存期間

解析対象:2012 年 10 月 31 日までの登録例 701 例のうち、一度も回答のない 3 例(No.637、673、677)を除く 698 例
起算日:登録日
イベント:死亡
打ち切り:生存例、追跡不能例は最終生存確認日で打ち切り

Kaplan-Meier 法による推定生存曲線

2012 年 12 月 4 日調査



解析対象	イベント (死亡)	打ち切り例の 最長追跡期間	最後のイベントが起こった 時点での無生存	生存期間中央値 (95%信頼区間)
698 例	5 例	2.69 年	158 例	推定不能

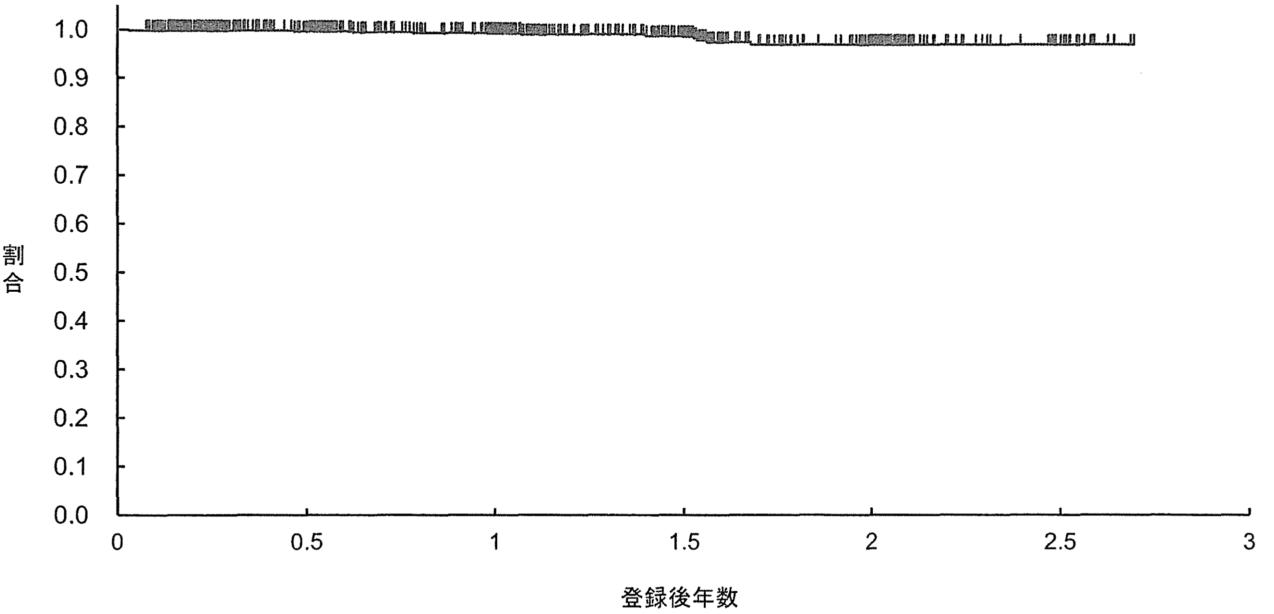
1 年生存割合 (95%信頼区間)	2 年生存割合 (95%信頼区間)
100% (100%−100%)	97.3% (93.5%−98.9%)

無再発生存期間

解析対象:2012 年 10 月 31 日までの登録例 701 例のうち、一度も回答のない 3 例(No.637、673、677)を除く 698 例
起算日:登録日
イベント:再発もしくは死亡
打ち切り:無再発生存例、追跡不能例は最終無再発生存確認日で打ち切り
※プロトコール 11.2.2.では「最終無再発生存確認日」で打ち切りとすると定義されている。しかし、本レポートでは無再発生存期間の標準定義に従い、「最終生存確認日」で打ち切りとした。(プロトコールマニュアル Ver.2.2 参照)主たる解析、最終解析時にはプロトコール定義通りの集計を行う。

Kaplan-Meier 法による推定無再発生存曲線

2012 年 12 月 4 日調査



解析対象	イベント (死亡・再発)	打ち切り例の 最長追跡期間	最後のイベントが起こった 時点での無再発生存	無再発生存期間中央値 (95%信頼区間)
698 例	10 例	2.69 年	177 例	推定不能

1 年無再発生存割合 (95%信頼区間)	2 年無再発生存割合 (95%信頼区間)
99.3% (98.0%−99.7%)	96.8% (93.9%−98.4%)

追跡調査のデータがアップデートされていない例

No.	群	施設名	最終生存確認日	担当医コメント
96	A	函館五稜郭病院	2011/10/19	なし

9. 転院患者一覧

No.	群	登録時施設名	転院先施設名	備考
426	B	静岡県立静岡がんセンター	宮城県立がんセンター	静岡県立がんセンター→宮城県立がんセンターへ転院

10. 監査委員会からの修正依頼案件

なし

11. QOL 調査票回収状況

QOL 調査参加施設：国立がん研究センター中央病院、神奈川県立がんセンター、静岡県立静岡がんセンター、
愛知県がんセンター中央病院

2013 年 8 月 12 日現在

全調査対象 512 例	登録時	術後 30 日	術後 90 日	術後 1 年	術後 3 年
		調査予定日前 20 例	調査予定日前 43 例	調査予定日前 139 例	調査予定日前 507 例
	回収済み 508 例	回収済み 483 例	回収済み 462 例	回収済み 359 例	回収済み 0 例
	未回収 2 例	未回収 3 例	未回収 2 例	未回収 5 例	未回収 0 例
	回収不能 2 例	回収不能 4 例	回収不能 1 例	回収不能 1 例	
	依頼せず 0 例	依頼せず 2 例	依頼せず 4 例	依頼せず 8 例	依頼せず 5 例

QOL 調査事務局からの報告

No.	調査時期	調査票	コメント
8	術後 1 年	回収不能	患者拒否（調査票を渡したものの回収できず）
45	術後 30 日	回収不能	記入・投函されたが、郵送段階で行方不明
49	登録時	回収不能	患者拒否*1
	術後 30 日 術後 90 日 術後 1 年 術後 3 年	依頼せず	登録時 QOL 調査欠損（患者拒否）のため
99	術後 1 年	依頼せず	患者拒否（調査票を渡して記入・投函を依頼できたもの、回収できず）
116	術後 90 日	回収不能	患者拒否（調査票を渡したものの回収できず）
	術後 1 年	依頼せず	患者拒否（調査票を渡して記入・投函を依頼できたもの、回収できず）
195	術後 30 日	回収不能	患者拒否（臨床試験に対する患者家族の理解が得られなくなったとのこと）
	術後 90 日 術後 1 年 術後 3 年	依頼せず	臨床試験に対する家族の理解が得られなくなった
196	術後 1 年	依頼せず	患者拒否（予定通り調査票を渡したものの、回収できず）
259	術後 1 年	依頼せず	患者拒否（調査票を渡して記入・投函を依頼できたもの、回収できず）
373	術後 30 日	回収不能	患者拒否（調査票を渡して記入・投函を依頼できたもの、回収できず）
449	術後 30 日	回収不能	患者拒否（調査票を渡して記入・投函を依頼できたもの、回収できず）
515	術後 1 年 術後 3 年	依頼せず	不安・うつ状態が出現し、調査依頼できず
536	登録時	回収不能	患者拒否（QOL調査票を渡して記入・投函を依頼したものの、回収できず）
	術後 90 日 術後 1 年 術後 3 年	依頼せず	登録時 QOL 調査欠損（患者拒否）のため
701	術後 30 日 術後 90 日 術後 1 年 術後 3 年	依頼せず	腹腔鏡下手術時に急性心筋梗塞を疑う心電図あり、胃切せず手術終了。心精査目的で転院となり試験中止

*1【データセンターコメント】A 群に割り付けられたが患者拒否あり。腹腔鏡下手術施行

CRF で「依頼できなかった」と報告された症例（調査予定日前に CRF が回収された症例を含む）

No.	調査時期	コメント
8	術後 1 年	外来日が調査日より遠い為、返送（郵送）されず、電話（留守電）と葉書により督促したが返事がない
195	術後 30 日	家族の臨床試験に対する協力が得られなくなりアンケート調査を主治医の判断で中止とする
	術後 90 日	術後合併症により入院が長引き、試験に対する家人の協力が得られず QOL 調査は中止となる

12. 他の JCOG 試験への登録患者一覧

JCOG1009/1010

No.	登録時施設名	JCOG1009 登録番号	JCOG1010 登録番号
602	静岡県立がんセンター	134	–
604	広島市立広島市民病院	–	1036

JCOG1104

No.	登録時施設名	JCOG1104 登録番号
562	神奈川県立がんセンター	13

研究成果の刊行に関する一覧表

別紙4

研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Nakamura K, Katai H, et al	A phase Ⅲ study of laparoscopy-assisted versus open distal gastrectomy with nodal dissection for clinical stage ⅠA/ⅠB gastric cancer(JCOG 0912)	Jpn J Clin Oncol	43(3)	324-327	2013
Nashimoto A, Katai H, et al.	Gastric cancer treated in 2002 in Japan: 2009 annual report of the JGCA nationwide registry.	Gastric Cancer	16(1)	1-27	2013
Ishida M, Kaai H, et al	Metachronous liver metastasis from early gastric cancer	J Gastrointest Surg	16(4)	837-341	2012
Gordon A, Sugihara K et al	Long-term comparison of laparoscopy-assisted distal gastrectomy and open distal gastrectomy in advanced gastric cancer	SurgEndosc	27(2)	462-470	2013
Inokuchi M, Sugihara K, et al	Long-term outcomes of Roux-en-Y and Billroth-I reconstruction after laparoscopic distal gastrectomy.	Gastric Cancer	16(1)	67-73	2013
Yoshikawa T, et al.	A prospective feasibility and safety study of laparoscopy-assisted distal gastrectomy for clinical stage I gastric cancer initiated by surgeons with much experience of open gastrectomy and laparoscopic surgery	Gastric Cancer	16(2)	126-132	April 2012
Yoshikawa T, Kunisaki C, Sakuramoto, S, Ito S, et al.	Laparoscopic or open distal gastrectomy after neoadjuvant chemotherapy for operable gastric cancer a randomized phase II traial. (Landscope Trial)	Jpn J Clin Onco	42(7)	654-657	2012
Kinoshita T, et al.	Laparoscopic transhiatal resection for Siewert type II adenocarcinoma of the esophagogastric junction: operative technique and initial results	Surg Laparosc Endosc Percutan Tech	22(4)	199-203	2012
Kinoshita T, et a	Laparoscopic proximal gastrectomy with jejunal interposition for gastric cancer in the proximal third of the stomach: a retrospective comparison with open surgery	Surg Endosc	27(1)	146-53	2012
Kunisaki C, et al	Surgical outcomes of laparoscopy-assisted gastrectomy versus open gastrectomy for gastric cancer: a case-control study.	Surg Endosc	26(3)	804-810	2012

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Sakuramoto S, et al.	Laparoscopy versus open distal gastrectomy by expert surgeons for early gastric cancer in Japanese patients short-term clinical outcomes of a randomized clinical trial.	Surgical Endoscopu	27(5)	1695-1705	2013
Yamashita K, Sakuramoto S, et al.	Survival outcome of laparoscopic gastrectomy for clinical early(cT1) gastric cancer.	Surgery Today	Published Online	Published Online	2012
Mochizuki Y, Kodera Y, et al.	Single-institute prospective trial of laparoscopy-assisted distal gastrectomy with systemic lymph node dissection for early gastric carcinoma.	Gastric Cancer	15(2)	124-130	2012
Kodera Y.	Introduction of laparoscopy-assisted distal gastrectomy: a tale of two cities.	Gastric Cancer	16(2)	115-117	2013

研究成果の刊行物・別刷

Japanese Journal of Clinical Oncology

Jpn J Clin Oncol 2013;43(3)324–327
doi:10.1093/jjco/hys220
Advance Access Publication 28 December 2012

A Phase III Study of Laparoscopy-assisted Versus Open Distal Gastrectomy with Nodal Dissection for Clinical Stage IA/IB Gastric Cancer (JCOG0912)

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A Phase III study was started in Japan to evaluate the non-inferiority of overall survival of laparoscopy-assisted distal gastrectomy with open distal gastrectomy in patients with clinical IA (T1N0) or IB [T1N1 or T2(MP)N0] gastric cancer. This study followed the previous Phase II study to confirm the safety of laparoscopy-assisted distal gastrectomy (JCOG0703) and began in March 2010. A total of 920 patients will be accrued from 33 institutions within 5 years. The primary endpoint is overall survival. The secondary endpoints are relapse-free survival, proportion of laparoscopy-assisted distal gastrectomy completion, proportion of conversion to open surgery, adverse events, short-term clinical outcomes, postoperative quality of life. Only a credentialed surgeon can be responsible for both open distal gastrectomy and laparoscopy-assisted distal gastrectomy.

Key words: gastric cancer – laparoscopic surgery – gastrectomy – clinical trial – Phase III

INTRODUCTION

The proportion of early gastric cancer accounts for only 15% in the western countries (1) while it does for more than 50% in Japan (2). In terms of the prognosis, the 5-year survivals of Stage IA and IB gastric cancer were reportedly as good as 93 and 87% (3). Especially for clinical stage IA gastric cancer which has no or only a few nodal metastases, less invasive procedure such as endoscopic mucosal resection or limited nodal dissection is recommended in the third version of Gastric Cancer Treatment Guideline in Japan (4). Laparoscopy-assisted gastrectomy (LADG) is another approach to reduce surgical invasion.

Since Kitano et al. (5) reported the first LADG in 1994, the number of patients who were treated by a laparoscopic technique has increased. However, laparoscopic surgery is still regarded as an investigational procedure in this guideline because the safety and feasibility was not well verified in a multi-institutional setting and there is no confirmatory randomized controlled trial to compare laparoscopy-assisted gastrectomy with open gastrectomy with a sufficient sample size. Thus, ODG is a standard procedure when tumors are located at distal stomach.

In our previous multi-institutional Phase II trial, we evaluated the safety of LADG with nodal dissection for clinical stage IA and IB gastric cancer (JCOG0703) (6). In this Phase II study, the proportion of patients with either anastomotic leakage or pancreatic fistula, the primary endpoint, was only 1.7% (3/173), which was much less than the prespecified threshold (8%). In addition, the overall proportion of in-hospital grade 3 or 4 adverse events was as low as 5.1%. We concluded that the safety of LADG was confirmed in this Phase II study, and now have launched a randomized controlled trial to compare the efficacy of LADG and ODG for clinical IA/IB gastric cancer.

The Protocol Review Committee of the Japan Clinical Oncology Group (JCOG) approved this protocol in February 2010 and the patient enrollment was started in March 2010. The approval by the institutional review board was obtained before starting patient recruitment in each institution. This trial was registered at the UMIN Clinical Trials Registry as UMIN000003319 (http://www.umin.ac.jp/ctr/index.htm).

PROTOCOL DIGEST OF THE JCOG0912

Objectives

The aim of this study is to confirm the non-inferiority of overall survival of LADG with nodal dissection with ODG for clinical stage IA (T1N0) or IB [T1N1 or T2(MP)N0] gastric cancer.

Study Setting

A multi-institutional randomized Phase III study.

Endpoints

The primary endpoint is overall survival in all eligible patients. Overall survival is defined as days from randomization to death from any cause, and it is censored at the last day when the patient was alive. The secondary endpoints are relapse-free survival, proportion of LADG completion, proportion of conversion to open surgery, adverse events, short-term clinical outcomes and postoperative quality of life (QOL).

Relapse-free survival is defined as days from randomization to relapse or death from any cause, and it is censored at the latest day when the patient is alive without any evidence of relapse. The proportion of LADG completion is defined as that of patients with whom LADG is completed without conversion to open surgery among all operated patients in the LADG arm. The proportion of conversion to open surgery is defined as the proportion of patients with conversion among the patients who are diagnosed before gastrectomy as clinical stage IA or IB. The short-term clinical outcomes consist of (i) the time from the end of surgery until the first episode of flatus, (ii) the proportion of patients requesting an analgesic on postoperative Days 5–10, (iii) the highest body temperatures during the first 3 days after the surgery and (iv) the highest body temperatures during hospitalization. Postoperative QOL is evaluated using EORTC QLQ-C30 and STO22. This QOL evaluation is performed only in four principal institutions due to the lack of resources in the other institutions. Primary analysis of QOL is performed using the global health status from EORTC QLQ-C30 in the 90th postoperative day.

Eligibility Criteria

Inclusion Criteria

(i) Histologically proven gastric adenocarcinoma.
(ii) Clinical stage IA (T1N0) or IB [T1N1, T2(MP)N0] according to the Japanese Classification of Gastric Carcinoma, Second English edition (7).
(iii) In case without preceding endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD), either 'cN1' or 'cN0 and no indication of EMR' is eligible.
(iv) In case with preceding EMR or ESD, the following conditions are fulfilled: (i) pathological findings require additional gastrectomy, (ii) within 91 days from EMR, (iii) no perforation by EMR and (iv) resection margin of EMR did not reach to the upper third of the stomach.
(v) Tumor located in the middle or lower third of the stomach, and curative resection is expected to be achievable by distal gastrectomy.
(vi) No invasion to duodenum.
(vii) Aged 20–80 years.
(viii) PS (ECOG) of 0 or 1.
(ix) A body mass index of <30.
(x) No history of upper abdominal surgery and no history of intestinal resection.
(xi) No prior treatment of chemotherapy or radiation therapy against any other malignancies.
(xii) Sufficient organ functions.
(xiii) Written informed consent.

Exclusion criteria

(i) Synchronous or metachronous (within 5 years) malignancies other than carcinoma *in situ*.
(ii) Infectious disease with a systemic therapy indicated.
(iii) Body temperature of 38°C or more.
(iv) Women during pregnancy or breast-feeding.
(v) Severe mental disease.
(vi) Continuous systemic steroid therapy.
(vii) Unstable angina pectoris or history of myocardial infarction within 6 months.
(viii) Uncontrollable hypertension.
(ix) Uncontrollable diabetes mellitus or administration of insulin.

(x) Severe respiratory disease requiring continuous oxygen therapy.

Randomization

After the confirmation of the eligibility criteria, registration is made by telephone, fax or web-based system to the JCOG Data Center. Patients are randomized to either the ODG arm or the LADG arm by minimization method balancing the arms with institution and clinical stage (IA/IB).

Treatment Methods

The ODG or the LADG is performed in respective arms. All procedures are same except for the surgical approach. The extent of nodal dissection is decided according to the surgical T and N stage which is based on the third version of the Gastric Cancer Treatment Guideline in Japan (4). D1 or more dissection is applied for clinical stage IA tumor and D2 dissection is applied for clinical stage IB tumor. For clinical T1 gastric cancer having 4 cm or more margin from the pylorus, pylorus-preserving distal gastrectomy is allowed. Bursectomy is not allowed but preservation of omentum and/or vagus nerve is discretionary. The reconstruction method is not specified in this study.

In the LADG arm, >6 cm of the mini-laparotomy incision is not allowed. If the intraoperative findings reveal a tumor stage of II or greater, the LADG is converted to an open surgery.

Only the surgeons credentialed by the study chair can be responsible for both LADG and ODG. In the ODG arm, the experience of 60 or more open gastrectomies is needed to be certified as a credentialed surgeon. In the LADG arm, the experience of 30 or more LADGs and the certification or its equivalent by the Japan Society for Endoscopic Surgery are needed. All the LADG procedures are centrally reviewed by photographs.

Follow-Up

Adjuvant chemotherapy with S-1 for 1 year is recommended for patients with curative resection and pathological stage II, IIIA or IIIB tumors.

All randomized patients are followed up for at least 5 years. Tumor markers, chest X-ray, upper gastrointestinal endoscopy and enhanced chest computed tomography is evaluated at least every year for the duration of the follow-up.

Study Design and Statistical Analysis

This randomized trial is designed to demonstrate that LADG is non-inferior to ODG in terms of overall survival. Some endpoints are adopted to evaluate the less invasiveness of LADG over ODG, but those endpoints are all considered to be exploratory. Thus, as long as the non-inferiority of LADG is confirmed, LADG will be concluded as one of the options of the standard treatments for clinical stage IA/IB gastric cancer.

According to the Schoenfeld and Richter's method (8), the planned sample size is 920 patients, with 460 patients per arm. We anticipate 5 years of follow-up after 5 years of accrual, ensuring at least 80% power with a one-sided alpha of 5% and a non-inferiority margin of 5% in terms of 5-year survival. This assumes an expected 5-year overall survival of 90% in each arm.

The patients who are randomized to the LADG arm and are converted to ODG are included in the LADG population for the efficacy analyses based on the intention-to-treat principle. In the safety analyses, they are also regarded as the LADG population if the surgery starts as LADG but changes to ODG in the middle of the surgery, while they are included in the ODG population if the surgery starts as ODG from the beginning.

Interim Analysis and Monitoring

We plan to conduct two interim analyses, taking multiplicity into account using the Lan-DeMets method with the O'Brien and Fleming type alpha spending function. The Data and Safety Monitoring Committee of the JCOG will independently review the interim analysis reports and stop the trial early if necessary. In-house monitoring will be performed every 6 months by JCOG Data Center to evaluate and improve the progress and quality of the study.

Participating Institutions (From North to South)

Hakodate Goryoukaku Hospital, Iwate Medical University, National Hospital Organization Sendai Medical Center, Yamagata Prefectural Central Hospital, Tochigi Cancer Center, National Cancer Center Hospital East, National Cancer Center Hospital, Tokyo Metropolitan Cancer and Infectious diseases Center Komagome Hospital, Tokyo Medical and Dental University Hospital, Cancer Institute Hospital of Japanese Foundation for Cancer Research, Toranomon Hospital, Kanagawa Cancer Center, Kitasato University School of Medicine, Yokohama City University Medical Center, Toyama Prefectural Central Hospital, Ishikawa Prefectual Central Hospital, Shizuoka General Hospital, Shizuoka Cancer Center, Aichi Cancer Center Hospital, Nagoya University School of Medicine, Fujita Health University, Osaka University Graduate School of Medicine, Kinki University School of Medicine, Osaka Prefectural Hospital Organization Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka Medical College, Kansai Medical University Hirakata Hospital, Hyogo Cancer Center, Wakayama Medical University School of Medicine, Shimane University School of Medicine, Hiroshima City Hospital, Fukuyama City Hospital, National Hospital Organization Shikoku Cancer Center, Oita University Faculty of Medicine.

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Conflict of interest statement

None declared.

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SPECIAL ARTICLE

Gastric cancer treated in 2002 in Japan: 2009 annual report of the JGCA nationwide registry

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Abstract
Background The Japanese Gastric Cancer Association (JGCA) started a new nationwide gastric cancer registration in 2008.
Methods From 208 participating hospitals, 53 items including surgical procedures, pathological diagnosis, and survival outcomes of 13,626 patients with primary gastric cancer treated in 2002 were collected retrospectively. Data were entered into the JGCA database according to the JGCA classification (13th edition) and UICC TNM classification (5th edition) using an electronic data collecting system. Finally, data of 13,002 patients who underwent laparotomy were analyzed.
Results The 5-year follow-up rate was 83.3 %. The direct death rate was 0.48 %. UICC 5-year survival rates (5YEARSs)/JGCA 5YEARSs were 92.2 %/92.3 % for stage IA, 85.3 %/84.7 % for stage IB, 72.1 %/70.0 % for stage II, 52.8 %/46.8 % for stage IIIA, 31.0 %/28.8 % for stage IIIB, and 14.9 %/15.3 % for stage IV, respectively. The

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proportion of patients more than 80 years old was 7.8 %, and their 5YEARS was 51.6 %. Postoperative outcome of the patients with primary gastric carcinoma in Japan have apparently improved in advanced cases and among the aged population when compared with the archival data. Further efforts to improve the follow-up rate are needed.
Conclusions Postoperative outcome of the patients with primary gastric carcinoma in Japan have apparently improved in advanced cases and among the aged population when compared with the archival data. Further efforts to improve the follow-up rate are needed.

Keywords Gastric cancer · Nationwide registry · 5-year survival rate (5YEARS) · Japan

Introduction

The registration committee of the Japanese Gastric Cancer Association (JGCA) started a new registration program in 2008 after a 10-year blank period, and we reported the 5-year follow-up data of the patients treated in 2001 [1]. The registration has been continuing, and here we report the results of those treated in 2002.

Materials and methods

Leading hospitals in Japan voluntarily downloaded and fulfilled the database provided by the JGCA and sent the anonymized data to the JGCA data center. The collected data were analyzed according to the previously reported methods [1].

Results

Data of 14,394 patients were collected from 208 hospitals; 126 (60.6 %) hospitals participated in both years, but 82 hospitals were new, which was a 10 % increase as compared to the previous year (13,067 patients from 187 hospitals). The geographic distribution of the registered patients among the 47 prefectures is illustrated in Fig. 1. In Tokyo, 2,332 patients per year were registered, followed by 1,464 in Osaka. Four other prefectures registered more than 500 patients. On the other hand, the number of registered patients was fewer than 100 in 10 prefectures, and there were no registered patients in 2 prefectures.

Patients with remnant stomach cancer, non-epithelial malignant tumor, and gastric cancer combined with malignant tumor of other organs were excluded. Patients who were treated by endoscopic mucosal resection were also excluded. Data of 768 patients lacked essential items. Consequently, data of the remaining 13,002 patients were used for the final analysis.

The results are shown in Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, and 28. Data given for each category of patients are: total number of patients, survival rates by year, standard error of 5YEARS, the number of direct death within 30 postoperative days, the number of patients lost to follow-up within 5 years, the number of 5-year survivors, and main cause of death, such as local and/or lymph node metastasis, peritoneal metastasis, liver metastasis, distant metastasis, recurrence at unknown site, other cancer, and other disease. Figures 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, and 17 provide cumulative survival curves of patients stratified by essential categories.

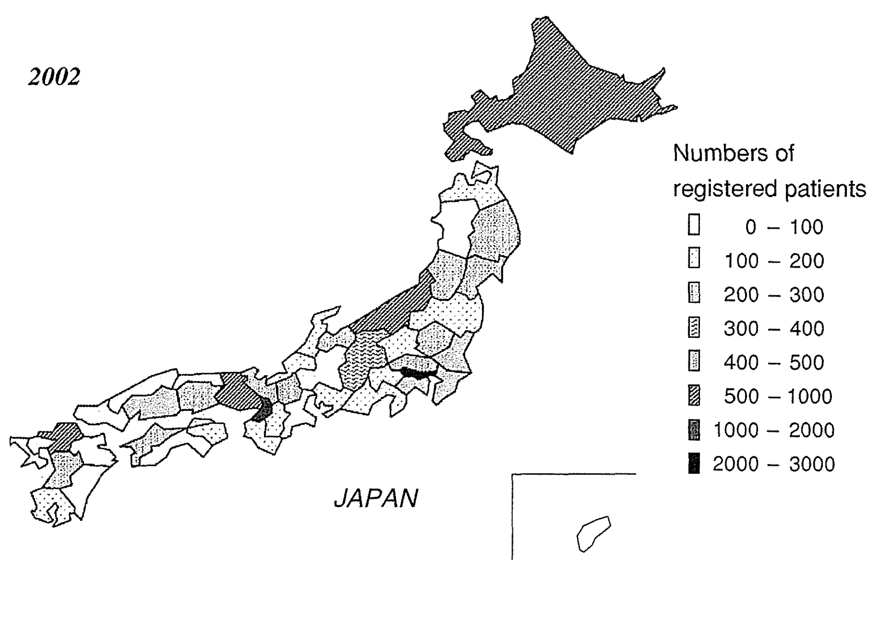

Fig. 1 Geographic distribution of registered patients by prefecture

Table 1 Primary cancer

Categories	No. of patients	Direct death	Lost f.u.	1 years (%)	2 years (%)	3 years (%)	4 years (%)	5 years (%)	SE at 5 years	Alive	Local rec.	Peritoneal	Liver rec.	Distant meta.	*R*	Other cancer	Other disease	Unknown
Primary cancer	13626	89	2233	88.1	79.6	74.5	71.2	68.9	0.4	7436	454	1483	388	243	322	167	567	333

lost f.u. lost to follow-up, *years(%)* years of cumulative survival rate, *SE* standard error, *rec* recurrence, *peritoneal* peritoneal recurrence, *R* recurrence of unknown site

Table 2 Resected cases and unresected cases and other surgeries

Categories	No. of patients	Direct death	Lost f.u.	1 year (%)	2 years (%)	3 years (%)	4 years (%)	5 years (%)	SE at 5 years	Alive	Local rec.	Peritoneal	Liver rec.	Distant meta.	*R*	Other cancer	Other disease	Unknown
Resected cases	13002	63	2173	89.8	81.6	76.5	73.1	70.7	0.4	7286	410	1283	357	215	278	158	539	303
Unresected cases	355	21	25	25.7	7.3	2.9	1.9	1.5	0.7	4	37	183	24	24	32	2	12	12

Table 3 Sex (resected cases)

Categories	No. of patients	Direct death	Lost f.u.	1 years (%)	2 years (%)	3 years (%)	4 years (%)	5 years (%)	SE at 5 years	Alive	Local rec.	Peritoneal	Liver rec.	Distant meta.	*R*	Other cancer	Other disease	Unknown
Male	8887	43	1464	89.7	81.4	76.1	72.5	70.0	0.5	4939	292	805	280	136	203	133	425	210
Female	4115	20	709	90.1	82.2	77.4	74.3	72.3	0.7	2347	118	478	77	79	75	25	114	93

Table 4 Age (resected cases)

Categories	No. of patients	Direct death	Lost f.u.	1 year (%)	2 years (%)	3 years (%)	4 years (%)	5 years (%)	SE at 5 years	Alive	Local rec.	Peritoneal	Liver rec.	Distant meta.	*R*	Other cancer	Other disease	Unknown
<39	297	0	50	93.0	83.2	82.1	80.2	79.4	2.4	190	5	36	1	4	4	0	1	6
40–59	3622	10	581	93.4	86.7	83.2	80.3	78.8	0.7	2316	78	327	67	61	64	28	42	58
60–79	8075	40	1279	89.1	80.5	74.8	71.4	68.9	0.5	4450	282	798	255	142	180	110	387	192
>80	1008	13	263	81.6	71.6	63.9	57.0	51.4	1.8	330	45	122	34	8	30	20	109	47

Table 5 Tumor location (resected cases)

Categories	No. of patients	Direct death	Lost f.u.	1 year (%)	2 years (%)	3 years (%)	4 years (%)	5 years (%)	SE at 5 years	Alive	Local rec.	Peritoneal	Liver rec.	Distant meta.	*R*	Other cancer	Other disease	Unknown
U	2681	18	434	87.3	77.5	71.1	67.1	64.3	1.0	1356	104	267	99	76	68	39	150	88
M	5182	8	881	93.6	88.4	84.4	81.7	79.7	0.6	3322	102	339	101	62	72	48	153	102
L	4249	28	766	90.3	81.8	76.8	73.2	70.8	0.7	2338	159	380	124	46	90	59	200	87
Whole	584	8	62	63.7	37.9	28.7	22.9	19.3	1.7	88	37	256	20	24	45	5	22	25

U upper third, *M* middle third, *L* lower third

Table 6 Macroscopic type (resected cases)

Categories	No. of patients	Direct death	Lost f.u.	1 year (%)	2 years (%)	3 years (%)	4 years (%)	5 years (%)	SE at 5 years	Alive	Local rec.	Peritoneal	Liver rec.	Distant meta.	*R*	Other cancer	Other disease	Unknown
Type0	6869	13	1294	98.1	96.1	94.0	92.1	90.2	0.4	4959	40	69	31	22	24	105	244	81
Type1	363	0	62	89.1	78.6	71.1	68.2	65.5	2.6	187	12	22	24	9	9	5	20	13
Type2	1717	21	291	87.0	75.8	68.1	63.0	60.4	1.2	798	86	147	118	49	61	20	105	42
Type3	2575	17	364	79.6	63.3	54.3	49.1	46.0	1.0	914	181	532	158	79	102	22	115	108
Type4	923	9	86	63.7	37.9	28.2	21.5	17.7	1.3	127	55	450	12	39	72	2	36	44
Type5	339	2	43	83.9	74.5	67.0	63.7	60.6	2.8	171	16	51	9	12	8	3	13	13