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進行胃がんの生存率を向上させる標準的治療法の開発に関する研究

平成２０年度　総括研究報告書

研究代表者　笹子　三津留

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研究代表者　笹子　三津留　兵庫医科大学外科　主任教授

研究要旨
腹腔鏡検査で播種を含めた遠隔転移がないことが確認された大型3型・4型胃がんに対して、手術および術後TS-1単剤による補助化学療法1年間投与を対照とし、試験アームはTS-1+CDDP療法を2コース後に対照と同様な手術および術後補助化学療法を行う新規治療法の優越性を検定する無作為化第Ⅲ相試験を実施している。本研究開始間もなく、術後補助化学療法が確立されて対照治療が変更となったため、実質的には2007年3月より登録が開始され、2009年2月末で80例が登録された。現在対象から除外している腹腔洗浄細胞診陽性例は予後がほぼ同等であることから対象に含める予定で試験計画の改定を申請中である。本改訂で年間10例程度の登録増を見込んでいる。参加施設も次年度より2施設増加することもあり、2010年中には予定症例数の過半数登録を目標とする。

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A．研究目的

全体では70%近い治癒率を達成した胃がんにおいて、依然10%程度の5年生存率にとどまっているスキルス胃がんあるいはそれに準ずる大きな3型胃がんの予後改善が本研究の目的である。スキルス胃がんは20代の若年者にも多く発生し、数多くの悲劇を生んできた。就労期の患者が多数を占める同疾患の予後改善の必要性は高く、その社会的な意義も極めて大きい。がん対策基本法にうたわれた75歳以下のがん生存率の改善にこの研究は極めて重要である。

B．研究方法

【研究形式】多施設共同の第Ⅲ相ランダム化比較試験（優越性試験）：プライマリーエンドポイントは全生存期間。

【研究対象】腹腔鏡検査を含めた臨床的検索で遠隔転移を伴わない、治癒切除可能な8cm以上の大型3型・4型胃がん症例。術前の画像診断で食道浸潤が3cm以下であり、登録時の年齢が20歳以上75歳以下、PS0,1、充分な経口摂取ができ、諸臓器の機能が良好で、患者本人の自由意志に基づく文書による同意を得ている患者。適格性を判断するために行う検査は総て日常臨床で通常行う検査であり、それらにより適格となった場合に、本試験に関する説明を行う。

【症例登録とランダム割付】JCOGデータセンターで中央登録し、施設、肉眼型、壁深達度、リンパ節転移程度を割付調整因子として最小化法にて割り付ける。対照群は手術＋術後 TS-1 による補助化学療法、試験治療は TS-1+CDDP による術前化学療法2コース＋手術＋TS-1による術後補助化学療法である。

【治療内容】試験治療：術前TS-1(3週投与1週休薬)＋CDDP(day8)による化学療法を2コース行う。治癒切除可能症例ではD2以上の郭清を伴う根治手術を行い、術後6週以内よりTS-1単独による化学療法を手術後1年を目安に実施する。対照群：割付後早期に試験群と同様な内容の手術

を行い、術後は試験治療と同じTS-1単剤による化学療法を1年間実施する。
【解析方法】全生存期間を用いた中間解析は予定登録数の半数が登録された後の最初の定期モニタリング時および全症例が登録を完了して治療が終了する時期の2度予定する。中間解析は適切な方法で多重性を考慮して行う。最終解析は、全例登録後3年経過時点で行う。
【予定症例数】予定登録数は316である。ただし、このうち16例は対照群が手術単独であった時期の症例であり、主たる解析はその後の300例中の適格例を用いて行うが、参考として全症例を含んだ解析も行う。
【実施施設】JCOG胃がん外科グループに所属する消化器がんの基幹施設37施設で実施している。
（倫理面への配慮）
本研究は手術単独を対照群とした第Ⅲ相試験として開始したが、ACTS-GC試験の結果をふまえて標準治療が変わったことから、倫理的観点から、それが判明した時点で即刻登録を中止し、プロトコールの改訂に取り組んだ。効果・安全性評価委員会の承認などの手続きを経て、改訂後のプロトコールで試験を実施している。本人に口答及び文章による説明を行い、文章による同意を得る。説明内容には、試験参加の自由、同意後の撤回の自由、質問の自由、個人情報の扱いなどが含まれ、試験の同意取得は、ヘルシンキ宣言、個人情報保護法、臨床研究に関する倫理指針の総ての要件を満たして行われている。

C．研究結果

プロトコール改訂前に16例を登録していたが、登録を一旦停止し、現在のプロトコールで2007年3月より登録を再開している。2009年3月現在81例を登録している。本年度では、月1-4例を登録したが、1年間で31例にとどまっている。予定の年間60例ペースにはかなり遅れているが、現在腹腔鏡所見で腹膜播種がないが腹腔洗浄細胞診で陽性であるために不適格となっていた症例を適格とする方向でプロトコール改訂を申請中である。これは、調査研究により、腹腔洗浄細胞診陽性例の予後は、スキルス胃がんにおいては陰性例と大きな差が無く、同じ治療ストラテジーを適応すべき対象と判明したことによる。現時点までに治療の完了した55例ではTRDは出ておらず、安全に試験は行われている。

D．考察

TS-1+CDDP＋根治手術は第Ⅱ相試験での評価において、第Ⅲ相試験の試験アームにふさわしいと考えられた。第Ⅱ相試験では、主たる目的がfeasibilityの確認であったことから、適格性を臨床・画像検査のみで決めたが、本第Ⅲ相試験では診断的腹腔鏡検査を実施した上で、腹膜播種が無く、洗浄細胞診陰性の症例のみを対象として実施している。しかし大型3型・4型胃がんでは洗浄細胞診陽性例の予後とそうでないものの予後には大きな差が無く、同じ治療法を適応すべきステージと考えられた。現在、洗浄細胞診陽性群（あるいは大網内など胃に近接した部位に限局した播種例）を本試験の対象として追加する改訂をJCOG効果・安全性評価委員会に提出している。この改訂が認められれば、年間10例程度の対照の増加は予想できる。

本研究開始時点ではコントロール群は手術単独であったが、ACTS-GCの結果を受けて両群に術後補助化学療法が行われることとなった。この改訂により、予後不良の対象に手術単独をコントロールとしていた元々のプロトコールよりは、登録の同意が得られやすいと期待されたが、患者の同意率は25%程度であり、手術を先送りすることを嫌う患者と逆に抗がん剤治療を先にして欲しいと希望する患者と両方があることもわかっている。説明同意の仕方を工夫するなどして、もう少し同意率を上げていきたい。そのためにも、施設毎に対象症例数、その内の試験登録数と非登録例における非登録理由の把握を引き続き実施していく予定である。少なくとも年間50例の登録を行っていきたい。
本研究は我が国において術前補助化学療法を評価する目的の初めての第3相試験であり、是非とも成功させる必要がある。今後の術前化学療法のあり方そのものに大きな影響をする試験であり、完遂の意義はきわめて大きい。

E．結論

TS-1+CDDP療法による術前化学療法は安全性と治療効果に優れ、遠隔転移のない予後不良進行胃がん症例に対する新しい治療法となりうるポテンシャルを持っている。現在第Ⅲ相試験を施行中で、症例数を増やす努力をさらに継続していく。

F．健康危険情報

現在まで登録された症例では該当なし。

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H. 知的財産権の出願・登録状況
該当なし。

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
Degiuli, M., Sasako, M., et al.	The standard D2 gastrectomy for advanced gastric cancer	M. Degiuli	Management of gastric cancer-recent advances	Edizioni Minerva Medica	Turin	2008	177-194

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
Sasako, M.	Surgery and adjuvant chemotherapy	International Journal of Clinical Oncology	13	193-195	2008
Sasako, M., Sano, T., et al.	D2 Lymphadenectomy Alone or with Para-aortic Nodal Dissection for Gastric Cancer	The New England Journal of Medicine	359	453-462	2008
Kurokawa, Y., Sasako, M.	Recent advances in chemotherapy and chemoradiotherapy for gastrointestinal tract cancers: adjuvant chemoradiotherapy for gastric cancer	International Journal of Clinical Oncology	13	479-482	2008
Sasako, M.	Adjuvant chemotherapy with 5-FU or regimens including oral fluoropyrimidine for curable gastric cancer	Gastric Cancer	12	10-15	2009
Kodera, Y., Ito, S., et al.	The number of metastatic lymph nodes is a significant risk factor for bone metastasis and poor outcome after surgery for linitis plastica-type gastric carcinoma	World J Surg	32	2015-2020	2008

笹子三津留	D2リンパ節郭清：適応と手技	手術	62	567-572	2008
笹子三津留	がん化学療法における外科医の役割	外科治療	98（増刊）	14-19	2008
吉川貴己、円谷彰、笹子三津留	VI. 抗悪性腫瘍薬の合併療法－総論と基本コンセプト－ 術前・術後補助化学療法	日本臨牀	67(増刊号1)	375－381	2009
伊藤誠二，笹子三津留	Upper G.I.Cancer食道・胃癌 胃癌 胃癌術後補助療法の新たな展開	癌と化学療法	35	1509-1511	2008
長 晴彦，吉川貴己，円谷 彰	【後期高齢者のがんの治療】 胃がん	MEDICO	39	245-248	2008
梨本 篤	術前化学療法後の手術に対する注意事項について	手術	62	234-241	2008
松井恒志、梨本篤	S-1/CDDP療法による術前化学療法が著効し根治手術が得られた進行胃癌の１例	癌と化学療法	35	499-501	2008

Ⅲ．研究成果の刊行物・別刷

「がん臨床研究事業」

研究代表者　笹子　三津留

THE STANDARD D2 GASTRECTOMY FOR ADVANCED GASTRIC CANCER

16

M. Degiuli, A. Vendrame, S. Muzio, M. Sasako, K. Maruyama

During the last decade the developments of gastric surgery have been focused on the technical viability and the oncological meaning of D2 nodal dissection. Two recent randomised trials, one from the Netherlands[1] and the other one from England[2], have showed a significantly higher rate of complications after D2 gastrectomy as compared to the standard D1 dissection, without highlighting main survival benefits. The Italian Gastric Cancer Study Group (IGCSG)[3] one arm – phase two multicentre prospective trial on D2 node dissection has documented, for the first time, mortality and morbidity rates comparable to those shown by eastern authors also in western patients. Moreover, preliminary results of the new IGCSG randomised trial on D2 versus D1 gastrectomy, have documented that the D2 gastrectomy can be a feasible and safe procedure also in western world, with low morbidity and mortality rates as compared to the classic D1 dissection, whenever it is performed in specialised high-volume centers by well trained surgeons, and if the pancreas is preserved during total gastrectomy requiring splenectomy. Interim analysis of this series has also shown a survival benefit for advanced cancers (T2-T3 and/or node positive patients) treated by D2 nodal dissection as compared to D1 procedure.

Most of the research on gastric cancer treatment is based on the evidence that while it is clear that gastric cancer develops distant metastasis rather seldom until the primary tumor becomes a T3 tumor, on the other hand the incidence of lymph node metastasis is already evident in early stages of the disease; in National Cancer Center Hospital series (1972-1991) lymph node metastasis is evident in 63% of T2 cancers! (Tab. 16-I)[4].

Therefore, local control of lymph node metastases through extended and super-extended node dissection during gastrectomy appears essential in order to cure the disease; it has been proved to prevent the metastatic spread of the disease, avoid the abdominal relapse and improve patient's survival.

SURGICAL TECNIQUE

Extent of resection: distal or total gastrectomy?

Nowadays, after a long debate concerning the indications to total gastrectomy (TG) *de principe*[5,6], most reference centres involved in the surgical treatment of gastric cancer have agreed that, according to the principles of the Japanese Research Society for the Study of Gastric Cancer, the indication to a subtotal (distal) or a total gastrectomy should depend on the site of the gastric cancer and on its macroscopic appearance, detected through the preoperative assessment (Borrmann's Type, Fig. 16.1). Following the criteria firstly described by the JRSGC and then assumed by the Italian Gastric Cancer Association (IGCA), a subtotal dissection is oncologically adequate when the proximal edge of the tumour is further than 3 cm from the cardia in case of early gastric cancer and well-circumscribed advanced gastric cancer (Bormann's type 1 and 2) or further than 6 cm in case of advanced gastric cancer of infiltrative type (Bormann's type 3). On the opposite, a total gastrectomy is required whenever those conditions are not respected or in case of linitis plastica (Borrmann's type 4), even if it seems mainly located in the lower gastric area. A total gastrectomy is also necessary in case of tumours located close to the greater curvature and above the Demel's point (watershed), because of the specific

Table 16-I. – Incidence of nodal, hepatic, and peritoneal metastases in % (A) and pathologic N-stage distribution (B) according to the tumor depth among 4683 patients who underwent laparotomy at NCCH in Tokyo between 1972 and 1991 (mm: mucosal and muscolaris mucosa; sm: submucosal; mp: muscolaris propria; ss: subserosal; se: serosal; si: surrounding organ invasion. Reproduced with permission of the author from Sasako[4].

A

Depth	Lymph node	Liver	Peritoneum	No. of patients
T1 mm	3.3	0.0	0.0	1,063
T1 sm	17.5	0.1	0.0	881
T2 mp	46.8	1.1	0.5	436
T2 ss	63.7	3.4	2.2	325
T3 se	79.9	6.3	17.8	1,232
T4 si	89.8	15.5	41.6	724
Total	47.7	4.5	11.5	4,683

B

Depth	N0	N1	N2	N3	N4
T1 mm	96.7	2.2	1.1	0.0	0.0
T1 sm	82.5	12.2	4.9	0.3	0.1
T2 mp	53.0	27.0	16.8	1.8	1.4
T2 ss	36.3	29.8	25.8	2.5	5.5
T3 se	19.5	24.4	40.1	6.9	9.2
T4 si	7.8	11.6	33.6	21.7	25.2
Total	51.7	15.7	20.3	5.5	6.8

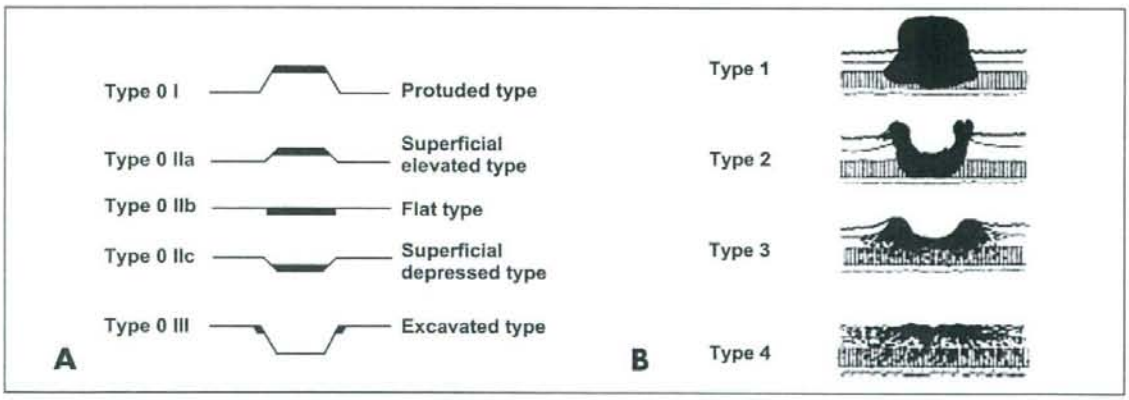

Fig. 16.1 – A) Subtypes of type 0 of Bormann's Classification: I: Protruded type; IIa: Superficial elevated type; IIb: Flat type; IIc: Superficial depressed type; III: Excavated type. B) Type 1: Polypoid tumors, sharply demarcated from the surrounding mucosa, usually attached on a wide base. Type 2: Ulcerated carcinomas with sharply demarcated and raised margins. Type 3: Ulcerated carcinomas without definite limits, infiltrating into the surrounding wall. Type 4: Diffusely infiltrating carcinomas in which ulceration is usually not a marked feature. Type 5: Non-classifiable carcinomas that cannot be classified into any of the above types. Reproduced with permission: "Japanese Classification of Gastric Carcinoma - 2nd English Edition", Gastric Cancer, 1998,1:10-24.

lymphatic drainage feeding into the splenic *hilum* and flowing along the splenic artery.

Anyway, we should not forget the main problem arising from the routine indication to partial gastrectomy in case of cancer of the lower part of the stomach: the quality of preoperative assessment of the proximal extension (mucosal or sub-mucosal) of the tumour. Despite the value of stepwise biopsy in detecting mucosal invasion and the usefulness of endoscopic ultrasonography in evaluating sub-mucosal or deeper extension of the tumour, the problem of the correct assessment of the proximal edge of the cancer is still under debate. Furthermore, consequently to the different biological pattern of

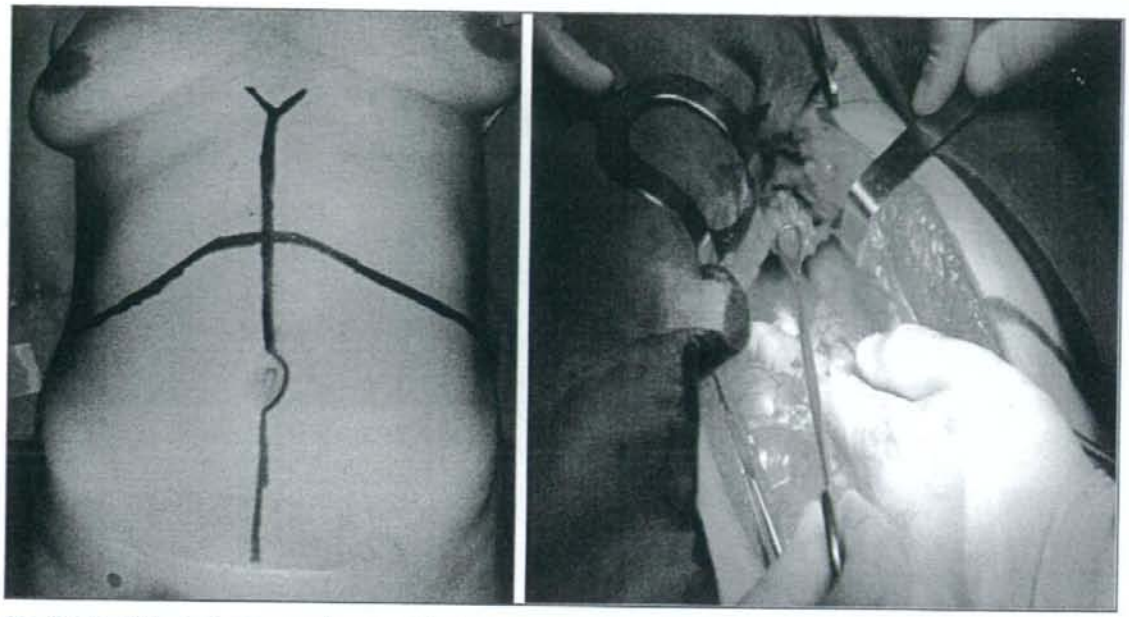

Fig. 16.2 – Abdominal incision and removal of xiphoid process.

intestinal- and diffuse-type cancers, some authors recommend to increase routinely the length of the proximal margin to at least 8 cm in case of diffuse cancer and to reduce it to 4 cm in case of intestinal type[7-9].

■ TOTAL D2 GASTRECTOMY

☐ Incision and evaluation

In most IGCSG reference centres the upper midline incision from the xiphoid process till 2-3 cm above the umbilicus is the incision of choice performed by the majority of surgeons. The bilateral sub-costal incision and the so-called Mercedes incision (bilateral sub-costal incision associated to a high upper midline incision over the xiphoid process) are other incisions performed in western countries and in Japan[10].

In order to improve the access to the cardias and the subphrenic area, the xiphoid process should be removed at the xipho-sternal junction (Fig. 16.2).

☐ Evaluation of the peritoneal cavity and peritoneal washing

A careful exploration of the peritoneal surface should be soon performed at the opening of the abdomen in order to exclude peritoneal spread of the cancer both on visceral and on parietal peritoneal leaves. At the same time the whole liver should be carefully examined at least also through intra operative ultrasonography in order to exclude unknown metastases. At the end of this intraoperative stage evaluation, the abdominal cavity is washed out with 100 mL of saline solution, while the stomach is carefully manipulated; the peritoneal lavage is then collected and immediately sent to the pathologist for intraoperative cytology (Fig. 16.3).

☐ 16B1 lymph node station sampling

The first surgical procedure entails a Kocher manoeuvre (Fig. 16.4), to access the para-aortic area

Fig. 16.3 – Peritoneal washing.

Fig. 16.4 – Kocker manouvre.

Fig. 16.5 – Interaorto-caval space: lymph node group 16B1.

(Fig. 16.5); this dissection allows a lymph node sampling of the group 16B1 (inferior para-aortic lymph nodes) for a frozen section analysis; the evidence of neoplastic cells at this level make the disease classified as M1 and any surgical treatment could not have a curative aim. On the other side, whenever a frozen section reveals no distant metastasis, a curative operation can be initiated.

☐ Dissection of the greater omentum from the transverse colon

Later (Figs. 16.6, 16.7), the greater omentum is dissected from the transverse colon together with the anterior sheet of the mesocolon (lesser sac). It is not sure that a complete removal of the greater omentum (omentectomy) and of the lesser sac (bursectomy) is necessary for T2 cancers; however it is absolutely necessary for T3 cancers which can involve the lesser sac. Many cancers that invade or are

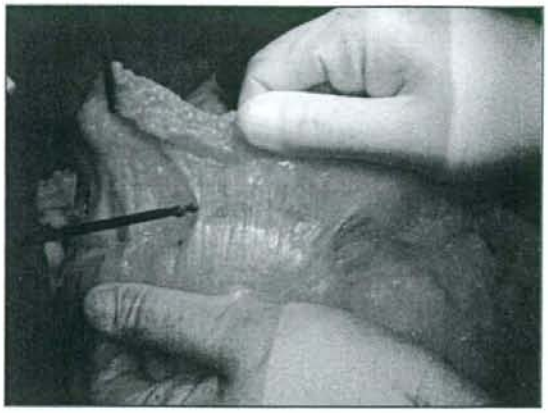

Fig. 16.6 – Dissection of the greater omentum and the anterior sheet of the transverse mesocolon.

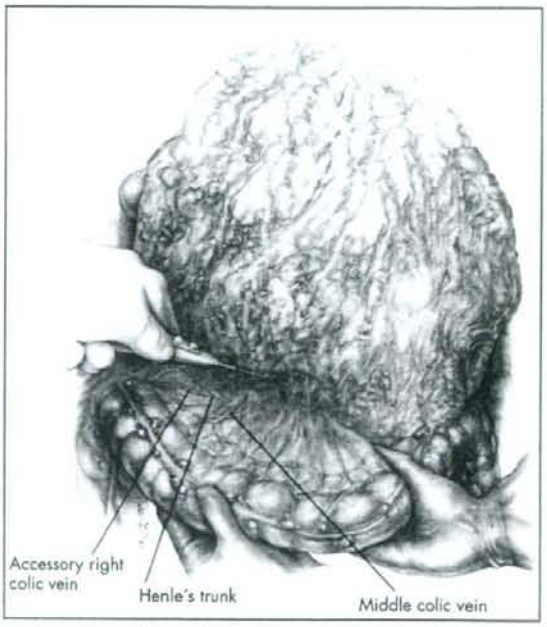

Fig. 16.7 – Dissection of the anterior leaf of mesocolon with omentum toward the pancreas. (Reproduced with permission of the author from Sasako[11]).

adherent to the anterior sheet of the mesocolon can be completely removed simply with the resection of the anterior sheet without resecting the transverse colon. The omentum is pulled up, while the first assistant spreads the transverse colon so that the operator can easily dissect the anterior sheet from the underlying tissue. This dissection is conducted from the hepatic flexure of the colon to the splenic one. The dissection is continued cranially from the colon toward the pancreatic body and tail and is

stopped close to the inferior border of the pancreas. On the right, the anterior sheet of the mesocolon continues on the duodenum and the head of the pancreas.

☐ Dissection of the right gastro-epiploic vein and pancreatic capsule

The dissection of the anterior sheet of the transverse mesocolon is continued towards right in order to find the right accessory colic vein which is followed cranially to the point where it joins Henle's trunk and the origin of the right gastro-epiploic vein (Fig. 16.8); this vein is ligated and divided at its origin. The middle colic vein, always outstanding on the mesocolon (Figs. 16.7-16.9), can lead this dissection towards Henle's trunk. A correct cranial traction of the omentum and the anterior leaf of the transverse mesocolon plays a fundamental role for this procedure (Fig. 16.10). As the mesocolon contains vessels emerging from behind the pancreas, the dissection of the anterior sheet of the mesocolon towards the pancreas leads to a plane behind it; therefore, at this point, the layer of dissection has to change from the posterior to the anterior surface of the pancreas. Several small vessels arising from behind the pancreas should be ligated and divided. The anterior leaf of the transverse mesocolon continues as "pancreatic capsule" which may contain lymphatic vessels and therefore should be dissected from the underlying pancreatic parenchyma and removed.

☐ Dissection of the right gastro-epiploic artery

The dissection of the pancreatic capsule is performed from the inferior to the superior border of the pancreas and from the middle of the pancreas body towards its head and the duodenum; the gastro-duodenal artery is found close to duodenum. This artery is followed caudally until the origin of the right gastro-epiploic artery, which is ligated and divided at its origin (Fig. 16.10). This dissection entails the removal of infrapyloric lymph nodes (group 6).

☐ Dissection of the left gastro-epiploic vessels

The dissection of the omentum and the anterior sheet of the transverse mesocolon continues to the left until the origin of the left gastroepiploic vessels is found, at the inferior border of the pancreas tail. The left gastroepiploic vessels will be accurately isolated, ligated and divided at their origin (Fig. 16.11); this dissection facilitates the complete removal of the left compartment of the lymph nodes of the greater curvature (group 4sb).

Fig. 16.8 – Right gastroepiploic vein.

Fig. 16.9 – Colic vessels and Henle's trunk.

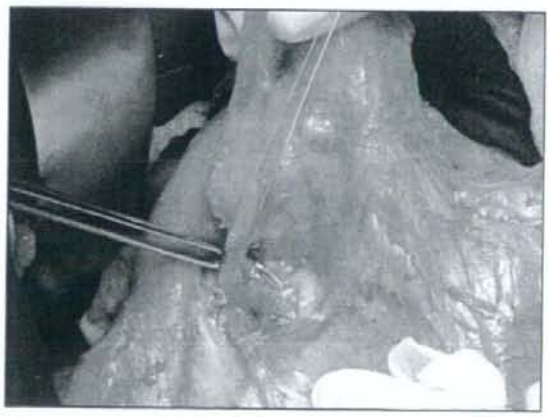

Fig. 16.10 – Right gastroepiploc artery.

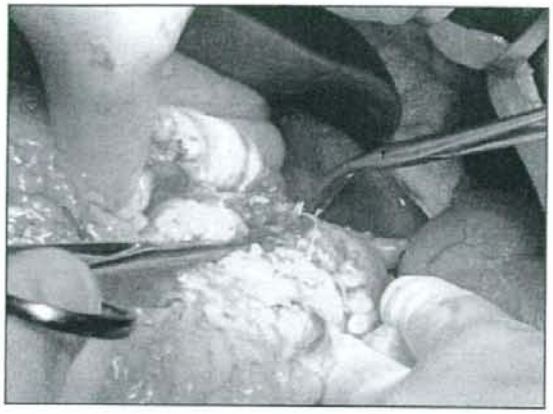

Fig. 16.11 – Left gastroepiploic vessels at their origin.

☐ Dissection of the lesser omentum

The dissection of the lesser omentum is a main step for a correct D2 lymphadenectomy. After the gastroepiploic artery is divided, the gastroduodenal artery is followed cranially until the common and proper hepatic arteries are recognised. There is usually a large lymph node lying in the space between the gastroduodenal and common hepatic artery and the superior border of the pancreas. Recent studies have documented that this node is often one of the sentinel node from tumors of the distal third of the stomach. The stomach is pulled down by the first assistant so that the lesser omentum and the serosa covering the esophageal hiatus are stretched. The lesser omentum is then divided 1 cm caudal to the attachment to the lateral sector of the liver (Figs. 16.12, 16.13), starting from the hiatus. In many cases an accessory left hepatic artery is found, arising from the left gastric artery (Fig. 16.14) and crossing the lesser omentum to the liver; in these cases it is necessary to preserve the accessory artery whenever it is possible, removing all the lymphatic tissue located around the origin of the left gastric vessel over the celiac trunk; in fact this tissue contains some of the lymph nodes of the station number 7.

The line of division of the peritoneal sheet of the lesser omentum just below the liver (Fig. 16.15) should be continued over the hepatoduodenal ligament, proceeding on the left side of the bile duct; the serosa of the ligament is then incised caudally toward the duodenum in order to discover the common hepatic artery at the level of its bifurcation in proper hepatic and gastro-duodenal arteries (Fig. 16.12).

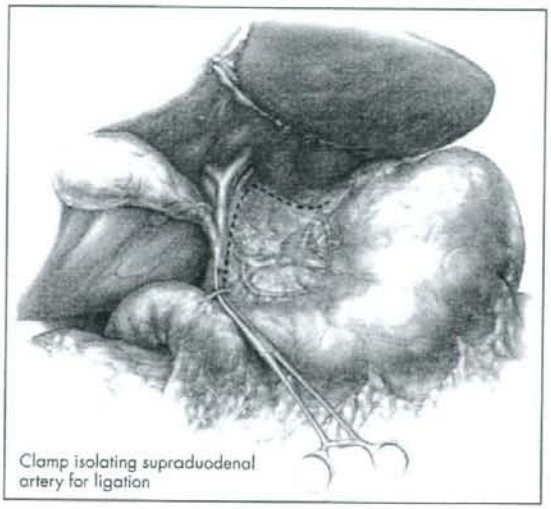

Fig. 16.12 – Incision line on lesser omentum. (Reproduced with permission of the author from Sasako[11]).

Fig. 16.13 – Lesser sack, dissection from esophageal hiatus.

Fig. 16.14 – Left epatic artery branching off from left gastric artery.

Fig. 16.15 – Lesser sack, dissection from the hiatus to the hepatoduodenal ligament.

Fig. 16.16 – Dissection of the right gastric vessels.

☐ Right gastric vessels isolation

The proximal ends of supraduodenal arteries are ligated at their origin from the gastroduodenal artery. Dissection of the hepato-duodenal ligament is continued to the bifurcation of the proper hepatic artery close to the hepatic hilum. The right and left hepatic arteries are recognised at this level and fatty connective tissue is dissected caudally and from the right to the left. The right gastric artery is found at this level, arising from either the gastroduodenal or proper hepatic artery in most cases. Sometimes the right gastric artery can arise from the left hepatic artery, expecially in case of low bifurcation of the proper hepatic artery (Figs. 16.12-16.17).

In this step of the procedure the first portion of the duodenum must be carefully dissected and divided in order to obtain the complete mobilisation of the stomach (Figs. 16.18, 16.19); this manouvre discovers the pancreatic surface and the loco-regional vascular structures originated from the celiac trunk. The pancreatic capsule must be completely removed together with the specimen (Figs. 16.20, 16.21), discovering the pancreatic parenchyma and the vascular and lymphatic tissue of its superior margin.

Before starting the dissection of the suprapancreatic nodes, lymph nodes along the left side and behind the portal vein are dissected, exposing the left and the posterior sides of the portal vein. Dissection of the suprapancreatic nodes, *i.e.*, common hepatic, coeliac, left gastric and splenic artery nodes, is now performed from right to left, from the portal vein to the middle of the splenic artery. The adipose tissue cranial to the pancreas contains many lymph nodes. This tissue is softly attached to the pancreatic parenchyma in most cases and therefore can be separated from the pancreas without difficulty. However in patients with a history of pancreatitis, dissection of suprapancreatic fatty tissue is difficult and the pancreas can be easily damaged, resulting in pancreatic leakages.

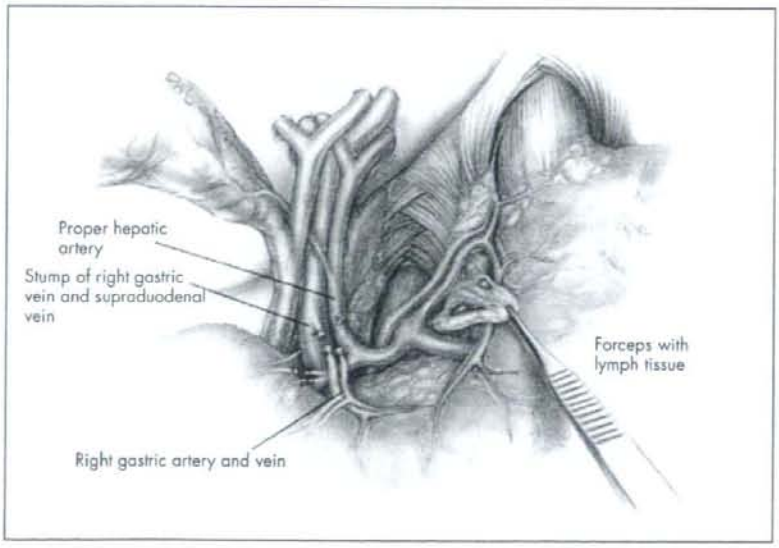

Fig. 16.17 – Division of the right gastric vessels. (Reproduced with permission of the author from Sasako[11]).

Fig. 16.18 – Duodenal dissection.

Fig. 16.19 – Duodenal division with a GIA device (Tyco srl).

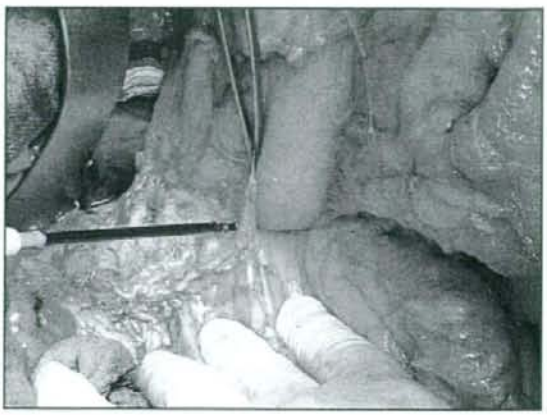

Fig. 16.20 – Removal of the pancreatic capsula.

glia should be preserved in case there are no obvious nodal metastases. The posterior border of this fatty tissue is the respective diaphragmatic crus on each side of the celiac artery. In about two thirds of the cases the left gastric vein is seen entering the portal vein close to the spleno-portal junction. The vein is then ligated and divided (Figs. 16.23, 16.24). After dissection of this tissue from the right crus, the right side of the celiac artery and the root of the left gastric artery can be recognized from its right side. The left gastric artery is sorrounded by thick nerve tissue, mainly celiac branches of the vagal nerves. Together with the nerve, the artery is ligated and divided near its origin (Figs. 16.23-16.25).

☐ Dissection of the left gastric vessels

Going towards left (Fig. 16.22), a left gastric vein crossing over the common hepatic artery or the splenic artery and entering the splenic vein is sometimes encountered during this stage of the procedure (about 30% of the cases). This vein should be ligated and divided near the superior border of the pancreas. The adipose tissue containing lymph nodes in this area is carefully dissected from the arteries and surrounding nerve tissue in a cranial direction. The nervous structures surrounding the arteries and including bilateral celiac gan-

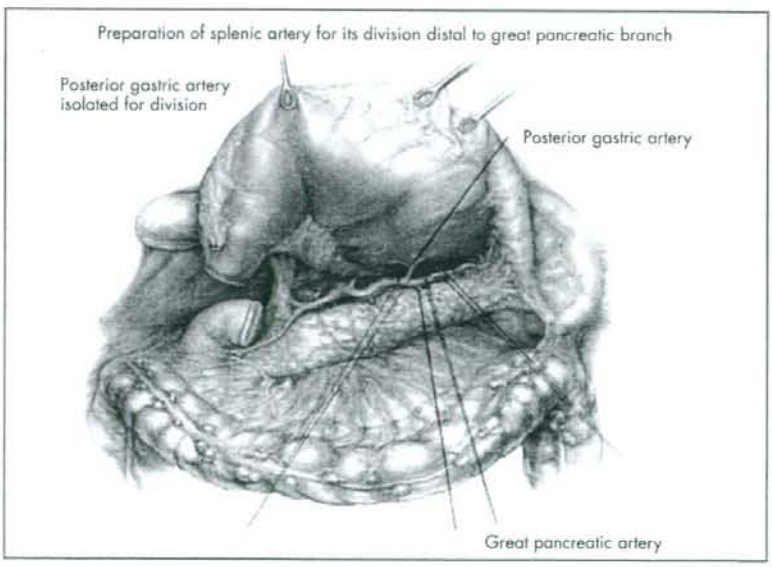

Fig. 16.21 – Removal of the pancreatic capsula (Reproduced with permission of the author from Sasako[11]).

☐ Spleen preserving D2 total gastrectomy (IGCSG technique)

Since the critical analysis of the two european randomised trials[1,2] documented that the increase of mortality and morbidity observed in the D2 arm was related to the pancreatectomy and splenectomy, usually performed as a routine step of the surgical standard treatment during total gastrectomy, several centres developed a different technique in order to preserve the pancreas and, in selected cases, also the spleen, during total gastrectomy.

Today there is not evidence of a survival benefit of splenectomy during total gastrectomy for cancer and data from JGCA randomised trial are not yet available. However, Japanese authors consider pancreas preserving D2 total gastrectomy with splenectomy as described by Maruyama (see below) the standard procedure for gastric cancer requiring total removal of the stomach; recently, following the worldwide discussion based on the several critical analysis of the recent European randomised trials, the Italian Gastric Cancer Study Group has developed a technique of total D2 gastrectomy that entails the preservation of the spleen in all cTNM T1 tumours, and in T2 and T3 cancers of the right part of the stomach, while requiring

Fig. 16.24 – Left gastric vein.

Fig. 16.22 – Final result of lymphatic dissection.

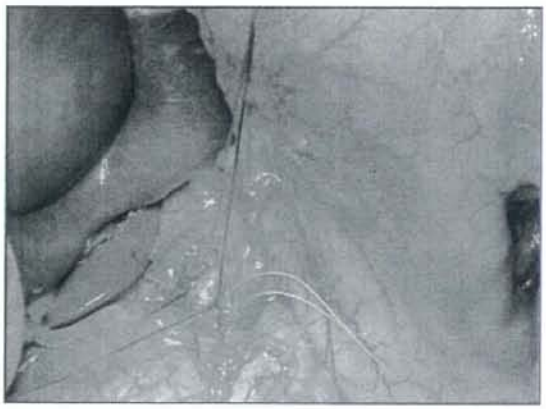

Fig. 16.25 – Left gastric artery.

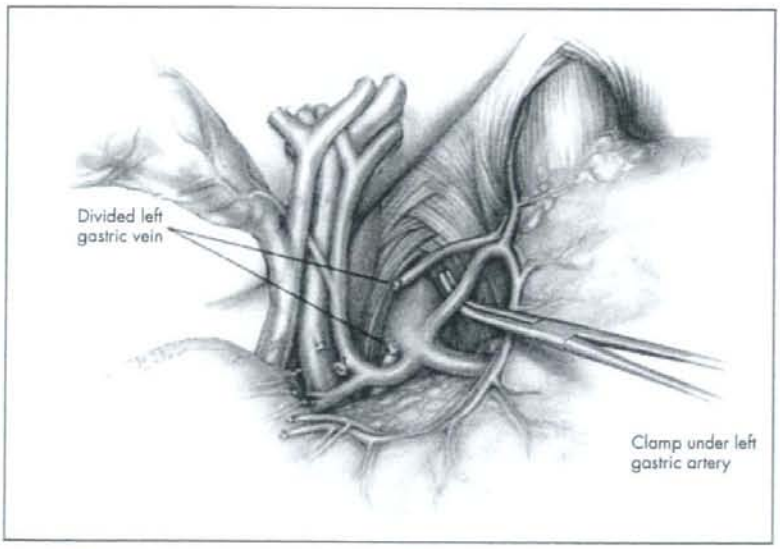

Fig. 16.23 – Dissection of left gastric vessels. (Reproduced with permission of the author from Sasako[11]).

splenectomy in all T4 cancers and in T2 and T3 tumors of the left part of the stomach. This technique will be described hereafter.

Following the lymphadenectomy on the left side of the celiac tripod, the dissection along the anterior surface of the splenic artery is continued until the posterior gastric vessels are encountered (Fig. 16.21); during total gastrectomy this artery should be dissected, ligated and divided at the origin of the splenic artery. All the lymph nodes along the splenic artery must be removed, starting from the proximal lymph nodes (group 11p). The dissection along the splenic artery continues until the pancreas tail, allowing the removal of all the lymph nodes of the distal group (group 11d).

Therefore, at the splenic *hilum*, we continue the dissection that was previously performed with the ligation and division of the left gastro-epiploic vessels, exposing the gastro-splenic ligament containing the short gastric vessels. During the surgical procedure with spleen preservation, the operation continues with the dissection of the short gastric vessels in order to completely remove all the lymph nodes of the group 4sa. This dissection is stopped on the left pericardial area. The stomach now can be further pulled up, exposing the left pericardial lymph nodes that should be complete removed dissecting the cardio-esophageal branch of the inferior left phrenic artery (Fig. 16.26), branching off to the left side of the cardia. The vagal trunks are divided at a suitable level based on the proximal extension of the tumor.

The continuous cranial pulling of the stomach by the first assistant (Fig. 16.21) facilitates to correctly expose the different structures to be dissected.

The abdominal esophagus is then divided with a safe surgical margin (Fig. 16.27) and the stomach is removed together with the loco-regional lymph node stations.

On the opposite, if splenectomy is performed (Fig. 16.28), the splenic artery should be divided distal to the origin of the great pancreatic artery (arteria pancreatica magna), which branches off at the same point of the posterior gastric artery, in order to improve blood supply to the tail of the pancreas as suggested by Sasako's modification of the original Maruyama's pancreas preserving D2 total gastrectomy. The splenic vein is preserved all along the surface of the pancreas and is ligated at pancreas tip of the tail, being necessary for the venous blood supply of the gland (see *pancreas preserving D2 total gastrectomy technique*).

Fig. 16.26 – Cardio-esophageal branch of the inferior left phrenic artery.

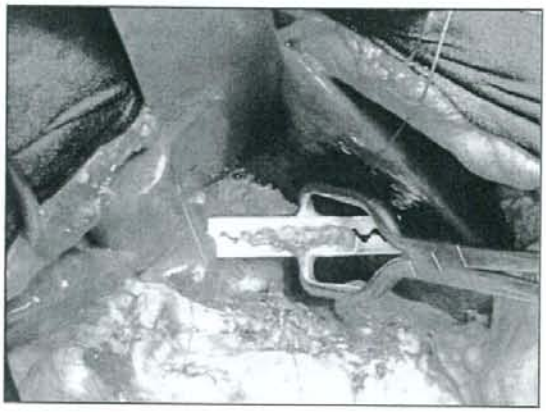

Fig. 16.27 – Esophageal section.

This kind of surgical treatment entails the removal of the following lymph nodes stations (according to the Japanese Gastric Cancer Association):

- group 1: right paracardial lymph nodes;
- group 2: left paracardial lymph nodes;
- group 3: lymph nodes along the lesser curvature;
- group 4 d, sb, sa: lymph nodes of the greater curvature (along the right and left gastro-epiploic vessels and the short gastric vessels);
- group 5: suprapyloric lymph nodes;
- group 6: infrapyloric lymph nodes;
- group 7: lymph nodes along the left gastric artery;
- group 8a: lymph nodes along the common hepatic artery (anterosuperior group);
- group 9: lymph nodes around the celiac artery;