MAURI IIVONEN

Jejunal Pouch Reconstruction after Total Gastrectomy for Gastric Carcinoma

University of Tampere
Tampere 2000
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ACADEMIC DISSERTATION
To be presented, with the permission of the Faculty of Medicine of the University of Tampere, for public discussion in the small auditorium of Building K, Medical School of the University of Tampere, Teiskontie 35, Tampere on September 22nd, 2000, at 12 o’clock.

University of Tampere
Tampere 2000
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List of original communications

This dissertation is based on the following original papers. The papers are referred to in the text by their roman numerals (I-IV)


Permission to reprint the original articles was kindly granted by S. Karger AG, Basel and Taylor and Francis AS, Oslo (www.tandf.no/surgery).

ABBREVIATIONS

ALAT alanine aminotransferase
ALP alkaline phosphatase
BI Billroth I gastroduodenostomy
BII Billroth II gastrojejunostomy
BMI body mass index (kg/m²)
CH4 methane
D2 lymphadenectomy dissecting R2 lymphnodes
GI gastrointestinal
H2 hydrogen
MCTT mouth-to-caecum transit time
N0 curative resection
ppm part per million
UICC Unio Internationalis Contra Cancrum
INTRODUCTION

The incidence of gastric cancer is decreasing in the Western world (Allum et al. 1989), but it is still the second commonest malignancy in the world. Tumours affect the upper part of the stomach more often than previously (Blot 1991, Longmire 1993) and the incidence of diffuse type carcinoma is increasing and thereby the need for total gastrectomy. Roux-en-Y oesophagojejunostomy is the preferred reconstructive method after total gastrectomy (Orr 1947, Donovan et al. 1982). Although the customary 50-cm long Roux-limb usually prevents alkaline reflux oesophagitis (Matikainen et al. 1982), other postoperative symptoms (Adams 1967, Olbe and Lundell 1987, Brägelmann et al. 1996) and malnutrition are still common problems after total gastrectomy. The Roux-en-Y reconstruction bypasses the physiological route through the duodenum, which may result in disturbances in digestion and absorption mechanisms. Some authors therefore prefer jejunal interposition over Roux-en-Y reconstruction (Kelly et al. 1954, Miholic et al. 1990).

The reservoir function of the stomach is lost after total gastrectomy, and therefore a variety of pouches have been introduced to alleviate postoperative symptoms and to increase eating capacity and improve nutrition (Hunt 1952, Lykidakis 1981). Different shapes of pouches made of jejunum or diverse parts of the colon have been used both with interposition (Cuschieri 1990, Fuchs et al.1995) and Roux-en-Y reconstruction (Nakane et al. 1995). GI surgeons are still searching for an optimal reconstructive method after total gastrectomy. Only few prospective randomised studies on pouches after total gastrectomy have been undertaken (Troidl et al. 1987, Nakane et al. 1995), and the results are conflicting.

Little is known of the emptying properties of the pouches (Heimbucher et al. 1994, Altomare et al. 1997). Bacterial overgrowth may be one important pathophysiologic mechanism behind malnutrition after total gastrectomy, but results concerning the incidence of bacterial overgrowth are conflicting (Bradley 1975, Olbe and Lundell 1987, Armbrecht at al. 1988). In addition to curative resection of the cancer, subsequent quality of life is of vital importance for the patient. Prospective long-term follow-up studies are
warranted to establish the best reconstructive technique for cancer patients undergoing total gastrectomy.

REVIEW OF THE LITERATURE

GASTRIC CARCINOMA

Carcinoma of the stomach is the second most common cancer in the world. It has been estimated that more than one million new cases were diagnosed world-wide in 1997, accounting for nearly 10% of all new cancers (Bozzetti et al. 1999, WHO 1997). More than 90 per cent of gastric cancers have been reported to be adenocarcinomas, the remainder being predominantly non-Hodgkin’s lymphomas or leiomyosarcomas (Fuchs and Mayer 1995). Gastric adenocarcinomas can be subdivided into two categories: an intestinal type and a diffuse type (Laurén 1965). These two forms appear to be involved with different epidemiologic and etiologic factors. Intestinal cancer tends to occur in the gastric antrum and is the type which predominates in areas of the world with a high incidence of gastric cancer. The diffuse type is usually found nearer the cardia; it occasionally occurs in young people and is associated with blood group A (McFarlane and Mundo 1997). Perhaps the most widely accepted hypothesis for the development of intestinal type gastric cancer is a gastritis-intestinal metaplasia-dysplasia-carcinoma sequence (Sipponen and Seppälä 1992, Sipponen 1994, Sipponen and Kahlos 1995). Helicobacter pylori may play a central role in the pathogenesis of gastric carcinoma (Sipponen and Kahlos 1995).

Despite a marked decline in the incidence of gastric carcinoma in many industrialised countries (Allum et al. 1989), cancer of the stomach remains the fifth most common cancer in the EU and the most common malignancy in China, Japan, Chile and Costa Rica (Levin 1989, Ajani et al. 1995, Bonenkamp et al. 1999). The incidence is also high in South America and in Eastern Europe. In 1997 the annual incidence In Finland among men
was 12.0 per 100,000 and 6.7 per 100,000 among women (Finnish Cancer Registry 2000) i.e. 472 new cases among men and 398 among women occurred. There has been a steady rise in the incidence of adenocarcinoma of the proximal stomach and the gastro-oesophageal junction, whereas the incidence of distal cancers has remained largely unchanged or has decreased slightly (Blot 1991, Longmire 1993). The incidence of adenocarcinoma of the gastro-oesophageal junction and gastric cardia has increased at a rate exceeding that of any other cancer, including melanoma and cancer of the lung (Fuchs et al. 1995). The intestinal type of carcinoma has decreased compared with the diffuse type (Kampschöer et al. 1989, Lauren and Nevalainen 1993, Wanebo et al. 1993). These epidemiological changes, despite the overall decline in the incidence of the disease and the fact that an increasing proportion of early lesions are found, underline the increasing need for total gastrectomy compared with gastric resection.
### Table I. TNM stage according to UICC (1987 classification)

<table>
<thead>
<tr>
<th>Stage IA</th>
<th>T1</th>
<th>N0</th>
<th>M0</th>
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<tbody>
<tr>
<td>Stage IB</td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
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<tr>
<td></td>
<td>T2</td>
<td>N0</td>
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<tr>
<td>Stage II</td>
<td>T1</td>
<td>N2</td>
<td>M0</td>
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<td></td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
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<td>T3</td>
<td>N0</td>
<td>M0</td>
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<tr>
<td>Stage IIIA</td>
<td>T2</td>
<td>N2</td>
<td>M0</td>
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<tr>
<td></td>
<td>T3</td>
<td>N1</td>
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<td>T4</td>
<td>N0</td>
<td>M0</td>
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<tr>
<td>Stage IIIB</td>
<td>T3</td>
<td>N2</td>
<td>M0</td>
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<td></td>
<td>T4</td>
<td>N1</td>
<td>M0</td>
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<tr>
<td>Stage IV</td>
<td>T4</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>any T</td>
<td>any N</td>
<td>M1</td>
<td></td>
</tr>
</tbody>
</table>

**Tis:** carcinoma in situ; **T1:** invasion to lamina propria or submucosa; **T2:** invasion to muscularis propria or subserosa; **T3:** tumour penetrates the serosa; **T4:** invasion to adjacent structures

**N0:** no regional lymph node metastases; **N1:** perigastric lymph node metastases within 3 cm of the primary tumour; **N2:** lymph node metastases more than 3 cm from the primary tumour or along the left gastric, common hepatic, splenic or coeliac arteries

**M0:** no distant metastasis

**M1:** distant metastasis
In Western countries, where routine screening is not cost-effective, gastric carcinoma is often diagnosed at an advanced stage and most patients present with symptoms such as abdominal pain, nausea, vomiting, loss of appetite and loss of weight (Wanebo et al. 1993, Arak 1996).

The two main prognostic factors in gastric carcinoma are lymph node involvement and the extent of tumour spread in the stomach wall (Fielding et al. 1984, Fuchs and Mayer 1995, Noguchi and Miyazaki 1996, Setälä 1998). The most frequently used classification for the extend of tumour spread in gastric cancer is the TNM (tumour, node, metastasis) stage classification recommended by UICC (Table I). Outside Japan advanced T3 and T4 lesions and lymph node metastases are found in 60% to 70% of patients (Ajani et al. 1995), only about 10 % having “early” (stage 0, stage IA) gastric carcinoma (Meyer et al. 1991).

In Sweden the 5-year relative survival rate increased significantly during the 1980s, having been 13.3 % among patients diagnosed 1960-1964 as against 19.4 % among those diagnosed in 1985-1986 (Hansson et al. 1999). In Japan the results of surgical treatment in gastric carcinoma have been better, with overall 5-year survival rate of about 50%, than in Western countries. One reason for this has proposed to be more radical lymphadenectomy (Kodama et al. 1981, Soga et al. 1988, Maruyama et al. 1989). Some recent studies from Western countries have shown benefit from extended lymphadenectomy (Shiu et al. 1987, Siewert et al. 1993, Viste et al. 1994, de Manzoni et al. 1996). However, a large, randomised study by the Dutch Gastric Cancer Group could not confirm this (Bonenkamp et al. 1999). Overall results in the West and in Asia may differ because the proportion of early cases (T1, T2) in the West is so limited (Fuchs and Mayer 1995), and by reason of the stage migration phenomenon (Bunt et al. 1995, Siewert et al. 1998). This means that the stage of the disease is underestimated because of limited lymphadenectomy. Furthermore, differences in diagnostic criteria
between Japanese and Western pathologists may play a role (Schlemper et al. 1997).

**SURGICAL TREATMENT OF GASTRIC CARCINOMA**

**Historical trends**

Descriptions of probable gastric carcinoma specimens date as far back as the millennium between 500 BC and 500 AD, but the story of gastric carcinoma may be said to start with Theodor Billroth’s first successful gastric resection for carcinoma in 1881 (Billroth 1881). Pean was the first to resect the stomach in 1879 for a tumour of the pylorus, but the patient died on the fifth postoperative day (Henley 1953). On 16th November 1880, Rydygier likewise performed a pylorectomy, but his patient died 12 hours later, and it was left to Billroth to perform and record the first successful gastric resection in man. This was in January 1881, when he excised an obstructing carcinoma of the pylorus and performed a gastroduodenostomy (Henley 1953). This was the first Billroth I operation. The Billroth II operation i.e. gastric resection with gastrojejunostomy was introduced in 1883. Hartman modified this procedure by performing an end-to side gastrojejunal anastomosis in 1898, but the unsuccessful outcome here and in attempts by other surgeons caused this technique to lapse. In 1911 Polya modified and re-introduced the Billroth II operation, which is why the operation is popularly known by this name. Polya’s anastomosis was retro-colic and many modifications have been made by prominent surgeons (Henley 1953).

The first partial gastrectomies were hardly more than pylorectomies, but as operative techniques improved, approaches became more radical and by 1940 the term “subtotal gastric resection” was taken to denote removal of the distal 66 to 75 per cent of the stomach. As the extent of gastric resection has increased, other methods of gastrointestinal anastomosis
have been adopted in addition to the Billroth I (end-to-end gastroduodenostomy) and Billroth II (side-to-side gastrojejunostomy) procedures. Of these, the most frequently employed after subtotal gastric resection for carcinoma has been the Hofmeister type of gastrojejunostomy (first performed by von Eiselsberg in 1888), in which the lesser curvature portion of the cut end of the stomach is closed and only the greater curvature portion anastomosed to the jejunum.

The first total gastrectomy was probably that performed by Conner in Cincinnati, but the patient succumbed (Conner 1887). Total gastrectomy was first successfully performed by Schlatter in Switzerland in 1897 (Schlatter 1897). The patient was a 56-year old woman, who lived nearly 14 months and died in consequence of secondary implants in the liver. Krönlein coined the term total gastrectomy in 1898. Brigham from San Francisco performed the first successful total gastrectomy in America, the patient surviving for 18 years (Herrington 1968). Up to 1929, 62 cases of total gastrectomy had been published, with a 53.8% operative mortality rate (Finney and Rienhoff 1929). The operative mortality in total gastrectomy was very high until the 1940s, when the introduction of antibiotics, blood replacement, and improved anaesthetic and surgical techniques helped to reduce the immediate surgical death rate. During this period total gastrectomy was proposed as routine treatment for all resectable carcinomas of the stomach. The approach was subsequently abandoned, however, since improved survival rates could not be demonstrated and operative mortality and the incidence of adverse side effects continued to be greater than after subtotal resection (ReMine et al. 1952). In most English language publications before the year 1970 the mortality rate reported after total gastrectomy has been more than 20% (Macintyre and Akoh 1991). Until the 1980s, total gastrectomy was used infrequently and was performed only in highly selected cases (Inberg et al. 1981).
Intestinal reconstruction after total gastrectomy was for the most part initially performed by suturing the oesophagus to the duodenum or to the loop of jejunum. The inevitable problem of regurgitation was solved with the adoption of Roux-en-Y oesophagojejunostomy in 1909 (Ikard 1989); other successful reports on this method were published in 1925 (Reid 1925). Most surgeons none the less continued to prefer the jejunal loop reconstruction with anastomosis between the two limbs to prevent reflux, until the 1940s, when several reports prompted renewed interest in the Roux-en-Y procedure. The concept of end-to-side oesophagojejunostomy was introduced in 1947 (Orr 1947) and Roux-en-Y oesophagojejunostomy is now the standard method of reconstruction after total gastrectomy.

**Total gastrectomy**

**Indications**

Complete surgical eradication of a gastric tumour, with resection of adjacent lymph nodes, is the only option for a cure in gastric carcinoma. Since resection of the primary lesion can also offer the most effective means of symptomatic palliation, abdominal exploration with curative intent should invariably be undertaken unless there is clear evidence of disseminated disease or other contraindications to surgery (Douglas and Nava 1985). There is general agreement that for some large gastric tumours involving more than one sector of the organ, total gastrectomy is required to achieve adequate clearance. Some surgeons have claimed that total gastrectomy is always preferable to partial resection irrespective of tumour size and type, and should be performed routinely (Shui et al. 1980, Meyer et al. 1989). Other authors hold that there is no evidence to support this practice and a mistake frequently made has been to equate total gastrectomy with a curative radical operation. The modern view of the latter alternative is a resection which guarantees an adequate tumour-free margin on both sides of the primary tumour and is accompanied by an
appropriate extended lymphadenectomy relevant to the exact location of the primary tumour. Thus, paradoxically, a total gastrectomy may not prove curative whereas a partial resection do so (Cuschieri 1989).

For patients with distal tumours, partial gastrectomy with resection of the adjacent lymph nodes appears to suffice. The original concept of total gastrectomy “de principe” was based primarily on the general confusion and difficulty concerning the level of radicality required when selecting resection lines at the stomach (Meyer et al. 1989). The margins of resection in gastrectomy for cancer have not always been adequate (Bozzetti et al. 1982). The recommended safety margin from the carcinoma to the resection line has been 6 cm proximally from the tumour, or at least 3 cm if the cancer is confined to the muscular layer (Bozzetti 1982). However, diffuse type carcinoma tends to grow under the mucosa and many authors thus recommend total gastrectomy for diffuse type carcinoma in every case (McNeer et al. 1974). Curative resection (R0 resection) is achieved if no tumour is left in the abdominal cavity and the resection margins are free of tumour in microscopic specimens (Hermanek 1995).

The proportion of total gastrectomies in one study from Germany involving 1420 patients and 22 surgical units was 37.1%, which was considered higher than in most Western or Japanese reports (Rohde et al. 1989). Another randomized trial comparing total and subtotal gastrectomy in cancer confined to the antrum demonstrated higher rates of morbidity and mortality after total gastrectomy with no difference in overall survival (Gouzi et al. 1989). In a recent multicentre randomized study both procedures had similar survival probability, and subtotal gastrectomy was associated with better nutritional status and quality of life. The authors suggested that subtotal gastrectomy should be the procedure of choice, provided that the proximal margin of resection falls in healthy tissue (Bozzetti et al. 1999). There are,
however, reports of cases in which distal gastric resection has achieved no advantage over total gastrectomy with pouch reconstruction (Buhl et al. 1995).

**Splenectomy and resection of adjacent organs**

Performing splenectomy and distal pancreatectomy as a part of surgery for gastric cancer has been criticised, mainly in view of the immunologic properties of the spleen (Griffin et al. 1995). Routine splenectomy for tumours not adhering to or invading the spleen has been associated with a higher complication rate and no clear survival benefit (Sugimachi et al. 1980, Suehiro et al. 1984, Brady et al. 1991, Fuchs and Mayer 1995). Significantly reduced 5-year survival, from 31 to 21 per cent has been observed after splenectomy among patients with stage II and III in a study involving 18 344 patients (Wanebo et al. 1997). In another recent randomized study comparing D1 and D2 lymphadenectomy, splenectomy and pancreatic resection were shown to be independent risk factors for surgical complications and to be associated with reduced survival in both D1 and D2 groups (Sasako 1997).

**Extended lymphadenectomy**

Studies on lymph nodes have revealed pathways of gastric lymph drainage (Wagner et al. 1991), and early metastases occurs through this lymph drainage network. Japanese Research Society for Gastric Cancer (JRSGC) divided lymph nodes into locations and allocated these into 4 groups. The location of the nodes are numbered from 1 to 16 (Figure 1 and Table II) and the groups are nominated from N1 to N4 (Table III). In the rules of the JRSGC the lymph node groups are related to the location of the primary tumour (JRSGC 1981). D 1 gastrectomy is defined as omentectomy and resection of the N1 nodes 3 cm around the primary tumour, and D 2 gastrectomy is defined as resection of
the omentum, anterior sheet mesocolon, pancreatic capsule and N2 lymph nodes related to the site of the tumour (van de Velde and Sasako 1998).

Extended lymphadenectomy is an essential part of gastric cancer surgery with curative intention in Japan and retrospective studies suggest that it may improve survival (Maruyama et al. 1987, Noguchi et al. 1989). Two small prospective trials, however, failed to demonstrate a benefit from extensive lymphadenectomy, which was associated with substantial morbidity (Dent et al. 1988, Robertson et al. 1994). The less extensive nodal dissection employed in Western countries probably results in an underestimation of the extent of the disease, generating lower rates of stage-specific survival (Bunt et al. 1995).

According to several recent randomised trials, long-term results after extended lymphadenectomy have shown no survival benefit when the entire patient population was analysed (Bonenkamp et al. 1995, Cuschieri et al. 1996, Siewert et al. 1998, Bonenkamp et al. 1999). On the other hand, the analysis of results in the German Gastric Cancer Study indicated an improved survival rate after extended lymphadenectomy in patient subgroups (Siewert et al. 1998). In UICC stage II tumours extended lymphadenectomy resulted in a marked improvement in 10-year survival, from 19.9% with standard lymphadenectomy to 49.2% with extended lymphadenectomy. The median survival time was 25.6 months after limited and 91.0 months after extended lymphadenectomy in this subgroup.
Figure 1. Lymph node location in gastric cancer according to the general rules for gastric cancer study in surgery and pathology (Bollschweiler et al.).

Table II. Numbering of lymph nodes according to JRSGC.

<table>
<thead>
<tr>
<th>Location</th>
<th>CMA</th>
<th>A, AM</th>
<th>MA, M</th>
<th>C, CM, MC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (N1)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
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<td></td>
<td>12</td>
<td>13</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

Table III. Grouping of lymph node locations according to the JRSGC

<table>
<thead>
<tr>
<th>Location</th>
<th>CMA</th>
<th>A, AM</th>
<th>MA, M</th>
<th>C, CM, MC</th>
</tr>
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<tbody>
<tr>
<td>Group 1 (N1)</td>
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<td>12</td>
<td>13</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

Group 4 (N4) consists of transverse mesocolon, para-aortic and perirenal nodes

(C=upper third, M=middle third, A=lower third). * dissection is optional
Morbidity and mortality
Surgery for gastric cancer patients entails high overall morbidity, related primarily to septic (12% to 34%) and major technical (10-18%) complications (Shchepotin et al. 1996). Allum and co-workers in 1989 reported overall mean operative mortality rates as high as 22% among surgeons undertaking even more than 9 total gastrectomies annually (Allum et al. 1989). The “acceptable” mortality rate ten years ago was regarded to be under 10 per cent (Meyer et al. 1989). In the recent years the operative mortality after total gastrectomy has been significantly reduced to the level of 6.6% (Sasako 1997) and an extremely low operative mortality rate of 0.6 percent has been observed (Maruyama et al. 1989). Some recent controlled clinical trials have shown that mortality and morbidity after total gastrectomy are on the same level as after limited surgical procedures (Hassler et al. 1986, Heberer et al. 1988, Gouzi et al. 1989, Macintyre and Akoh 1991).

Oesophagojejunostomy leakage constitutes one of the difficult problems in gastric cancer surgery, currently encountered on average in 3% to 7.4% of patients (Jatzko et al. 1992 and Sowa et al. 1992). In Finland leakage rates from 2% to 10.8% after total, near-total and proximal gastrectomies have been reported (Inberg et al. 1981, Saario et al. 1986, Saario et al. 1987, Ovaska et al. 1989). This complication is usually attributable to technical problems or nutritional/metabolic disorders. Leakage rates as low as 0.8% have been reported using a special surgical technique (Shchepotin et al. 1996). Mortality after anastomotic leakage is about 10% in Japan, but was 30% in a Dutch trial (Bonenkamp et al. 1995). The higher average age of Western gastric cancer patients, the frequent occurrence of cardiopulmonary complications and the different means of treating leakage have been considered as reasons for the difference (Bonenkamp et al. 1995). Oesophagojejunostomy may be difficult to perform by reason of the deep and narrow operative field. To obtain better
vision thoracoabdominal incision is sometimes needed for proximal carcinomas (Hölscher et al. 1989).

Since the introduction of the EEA® stapler by the US Surgical Corporation (Norwalk, Connecticut, USA) in 1967, many surgeons have used a variety of staplers for performing anastomosis (Huttunen et al. 1982, Walther et al. 1986, Moreno-Gonzales and Carboni 1988, Walther et al. 1989b, Fujimoto et al. 1991). Oesophagojejunal anastomosis may be performed by either end-to-side or end-to-end technique. In a prospective study of anastomotic failure following total gastrectomy, Viste and co-workers (1987) showed the risk of anastomotic leakage to be 2.4 times greater for hand-sutured than for stapled anastomoses, whereas Seufert and colleagues (1990) found no significant differences between the groups in operating time, morbidity, hospital stay or anastomotic leakage rate. Likewise, a large series of 379 patients comparing stapled and manual suturing (Fujimoto et al. 1991) showed no difference in the incidence of anastomotic leakages or stenosis. So there are no data at the moment available from clinical trials, which would prove one suture technique superior to other available methods (Schardey et al. 1997). Balloon dilatation (Chung et al. 1987) and local application of lidocaine (Kumashiro et al. 1990) have been suggested to help in performing a stapled anastomosis safely and easily. Using too large a stapler there is a risk of tearing the oesophageal wall, while too small may lead to a stenosis (Chassin et al. 1984).

Viste and colleagues (1987) found a tendency towards reduced anastomotic failures in patients receiving systemic antibiotic prophylaxis compared with those without. Schardey’s group (1997) in their prospective, randomised, double-blind placebo-controlled study showed for the first time that topical antibiotics reduced the anastomotic leakage rate after total gastrectomy. In this study polymyxin B, tobramycin, vancomycin and amphotericin B were used orally from the day before the operation until the
seventh postoperative day. The leakage rate was 10.6% in the placebo group compared with 2.9% in the decontamination group.

**RECONSTRUCTION METHODS AFTER TOTAL GASTRECTOMY**

After the first successful total gastrectomy in 1897 Schlatter reconstructed the alimentary tract continuity by an end-to-side oesophagojejunostomy (Schlatter 1897). Many of the early pioneers of total gastrectomy employed oesophagoduodenostomy (Waugh and Hood 1954) or performed a loop oesophagojejunostomy (Ikard 1989). These modes of approach were commonly used for 50 to 60 years, during which time operative mortality rates of 22% - 50% were reported (Allen 1938, Herter and Auchincloss 1957, Fly et al. 1958, Barber et al. 1963). The high operative risk and malnutrition frequently observed after the operation gave total gastrectomy an unfavourable reputation.

In many patients oesophagoduodenostomy may prove unfeasible for anatomical reasons and both this approach as well as loop oesophagojejunostomy frequently cause alkaline reflux oesophagitis. The technique of loop oesophagojejunostomy was modified by Hoffman (1922), who added a small side-to-side jejunojejunostomy between the two limbs of the jejunal loop. This afforded a partial bypass of the duodenal contents and reduced the incidence of reflux oesophagitis.

There are more than 50 described operations for intestinal reconstruction following total gastrectomy (Lygidakis 1981, Lawrence 1996). The major concern after total gastrectomy relates to the integrity of the oesophageal anastomosis. Later postoperative problems associated with reconstruction are nutritional state and quality of life issues, that are affected by aspects of the reconstruction other than the oesophageal anastomosis.
itself. The main categories of reconstruction following total gastrectomy are restoration of intestinal continuity without preservation of the duodenal food-passage (Roux-en-Y oesophagojunostomy) and restoration of intestinal continuity with preservation of the duodenal passage (jejunal interposition). Operations in either category may be combined with the construction of an enteric pouch or gastric reservoir to simulate the reservoir function of the normal, intact stomach (Figure 2).

Figure 2. Types of reconstruction after total gastrectomy: a. jejunal interposition, b. jejunal interposition with a pouch, c. Roux-en-Y, d. Roux-en-Y with a pouch.
**Roux-en-Y method**

The Roux-en-Y oesophagojejunostomy has become the most frequently used reconstruction method throughout the world (Herfarth et al. 1987, Thiede et al. 1987, Troidl et al. 1987). The procedure was introduced by César Roux, a Swiss surgeon and professor, in 1893 (Roux 1893). Originally after gastric resection the limb was placed retrocolically. Roux-en-Y gastrojejunostomy promptly fell into disfavour because of a recurrent complication i.e. anastomotic ulceration (Ikard 1989).

The idea of using Roux-en-Y reconstruction after total gastrectomy was introduced as early as 1909 (Waugh and Hood 1953). Despite a new report in 1925 on the use of that anastomosis (Reid 1925), most surgeons continued to prefer loop oesophagojejunostomy with anastomosis between the two limbs to prevent reflux. In the 1940s several reports once again drew attention to Roux-en-Y anastomosis and in 1947 (Orr 1947) end-to-side oesophagojejunostomy was introduced. The primary consideration in constructing a Roux-en-Y limb is the maintenance of adequate blood supply. Vasa recta vessels must be divided, and blood supply occurs through an intact vascular arcade. The classic distal Roux-en-Y limb is mobilised by dividing two or three vasa recta beyond the first, which is preserved (Ikard 1989).

The main objective in choosing the Roux-en-Y method after total gastrectomy is to prevent bile from refluxing to the oesophagus. Bile may cause mucosal damage to the oesophageal mucosa i.e. alkaline oesophagitis (Kivilaakso et al. 1981, Matikainen et al. 1982, Liedman et al. 1996).

In 1924 the suggested length of the Roux-en-Y limb was only 7.5 cm and the recommended length has steadily and markedly increased over time. Wells and Johnston (1956) suggested a length of 20-25 centimetres in the 1950s. The length of at least 35 has been shown to prevent alkaline reflux.
oesophagitis (Donovan et al. 1982). The great majority of experienced surgeons today use limb lengths of 40 to 60 centimetres.

**Jejunal interposition**

Jejunal interposition offers at least theoretical advantages over the Roux-en-Y reconstruction (Herfarth et al. 1987, Woodward and Hocking 1987). Preservation of the duodenal passage has been shown to be associated with enhanced postprandial release of hormones and regulatory peptides (Heil et al. 1981, Longmire and Beal 1952, Henley 1953). Enteroglucagon, which is released after contact of undigested nutrients with jejunal mucosa, reaches higher serum levels after partial and total gastrectomy bypassing the duodenum (Heil et al. 1981). Kelly and colleagues (1954) suggested that deficient pancreatic secretion secondary to inadequate stimuli and inadequate mixing of food with biliary and pancreatic secretions are due to impaired assimilation of dietary fat and emphasised the importance of the passage of food through the duodenum.

Some nonrandomized, retrospective studies have suggested superior performance of jejunal interposition compared with Roux-en-Y oesophagojejunostomy with respect to nutrition and ability to resume work (Miholic et al. 1990). However, interposition of a jejunal segment between oesophagus and duodenum has been considered a high-risk procedure compared with other reconstructions (Moreno-Gonzales et al. 1988). Furthermore, a recent randomized comparison between jejunal interposition with pouch versus Roux-en-Y pouch reconstruction could not show any significant difference between the two operation methods (Fuchs et al. 1995). The conclusion was that patients with gastric cancer after total gastrectomy do not benefit from reconstructing the duodenal passage by a jejunal interposition with pouch regarding their postoperative quality of life when compared to the
widely used and technically less demanding Roux-en-Y reconstruction with pouch.

**CONSEQUENCES OF TOTAL GASTRECTOMY**

Malnutrition, assessed in terms of weight loss, has been regarded as the most frequent complication after total gastrectomy (Adams 1967). On one hand postgastrectomy postoperative symptoms like early satiety, dumping and anorexia may reduce amount of ingested food and cause malnutrition (Adams 1967, Olbe and Lundell 1987, Sategna-Guidetti and Bianco 1989). On the other hand total gastrectomy causes many defects and disorders in digestive physiology. Digestion and absorption of nutrients is altered in many different mechanisms. Grinding of foodstuffs, and mixing with digestive enzymes is changed. Timing in secretion of bile and digestive enzymes is altered, gastric reservoir function is lost, hormonal and nervous regulation of the gastrointestinal canal is disturbed. Intestinal motility might be changed and normal bacteriology of the small intestine is altered. In addition, different modes of reconstructions – pouch or no pouch / duodenal passage or no duodenal passage - may have different effects in this respect. The pathophysiological mechanisms of malnutrition after total gastrectomy are presented in Table IV.
### Table IV. Pathophysiological mechanisms of malnutrition after total gastrectomy

<table>
<thead>
<tr>
<th>DECREASED INTAKE</th>
<th>MALDIGESTION AND MALABSORPTION</th>
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<tr>
<td>- lost reservoir function</td>
<td>- inadequate mixing</td>
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<td>- postoperative symptoms</td>
<td>- inadequate micelle formation</td>
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<td>- decreased appetite</td>
<td>- inappropriate pancreas stimulation</td>
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<td></td>
<td>- fat malabsorption</td>
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<td></td>
<td>- loss of antrum</td>
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<td></td>
<td>- bacterial overgrowth</td>
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<td></td>
<td>- duodenal bypass (Roux-en-Y)</td>
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<td></td>
<td>- vagotomy</td>
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<td></td>
<td>- increased motility</td>
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<td>- mucosal lesions</td>
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<td>- lack of gastric acid</td>
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<td>- lack of gastric lipase</td>
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<td>- lack of intrinsic factor</td>
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<td>- calcium, vitamin D, Fe</td>
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<td>malabsorption</td>
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<td></td>
<td>- lactose intolerance</td>
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<td></td>
<td>- villus atrophy</td>
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Many of these mechanisms behind postoperative symptoms and malnutrition are purely understood, and the relative significance of each of them should be known in order to find the best reconstruction method for the patients and to develop postoperative supplement therapy.

To alleviate the symptoms and to avoid malnutrition by increasing the volume of food ingested, various pouch reconstructions have been advocated (Hunt 1952, Lygidakis 1981, Herfarth et al. 1987, Nakane et al. 1995).
Postgastrectomy symptoms

Huguier and colleagues (1976) studied the functional results of different reconstructive procedures after total gastrectomy in 181 patients and reported the following overall incidence of functional disorders during the first postoperative months: jejunal distension 22%, dumping syndrome 20%, dysphagia 26%, reflux 18%, diarrhoea 41% and anorexia 31%.

Heartburn, alkaline reflux, and regurgitation

Oesophagitis after total gastrectomy would appear to be secondary to duodeno-oesophageal reflux (Helsingin 1959, Morrow and Passaro 1976, Matikainen et al. 1982). Stein and associates (1994) found intestino-oesophageal reflux to occur particularly during the postprandial period and the early morning hours in patients after subtotal or total gastrectomy. Roux-en-Y oesophagojejunostomy has been the preferred reconstructive procedure after total gastrectomy because it prevents postoperative alkaline reflux oesophagitis (Matikainen et al. 1982, Herfarth et al. 1987, McCulloch 1987, Gouzi et al. 1989). Twenty eight per cent of patients with benign disease or no cancer at the anastomosis have been reported to have moderate to severe oesophagitis: 100% after simple oesophagojejunostomy, 57% after oesophagoduodenostomy and 2.4% after Roux-en-Y oesophagojejunostomy (Schrock and Way 1978). Although reflux oesophagitis is not usually seen in connection with Roux-en-Y reconstruction after total gastrectomy (Buhl et al. 1990), there are reports of patients suffering from postoperative reflux oesophagitis as a subsequent complication (Salo and Kivilaakso 1990, Marshall et al. 1999). It is to notice that in the study of Marshall and co-workers most of the patients with oesophagitis after Roux-en-Y reconstruction appeared to have recurrent cancer.
A 35-cm to 50-cm length of small intestine between the oesophagojejunal and entero-entero anastomosis has been proposed to be necessary to prevent reflux of bile to the oesophagus (Donovan 1982, Hubens et al. 1989). Length of about 20 cm might be necessary in prevention of alkaline reflux when the continuity of the alimentary tract is re-established with an isoperistaltic loop between oesophagus and duodenum ( ). Construction of oesophagojejunoplication has also been suggested to prevent mechanically the reflux of the intestinal contents into the oesophagus after total gastrectomy (Stier et al. 1994).

**Roux-en-Y stasis syndrome and early satiety**

The Roux-en-Y procedure may itself be in part responsible for the post-prandial fullness experienced by most patients after removal of their stomach. The Roux limb may act as an area of functional obstruction when isolated from the pacemaker of the small bowel located in the bulb of the duodenum. This so-called Roux-en-Y syndrome is characterised by chronic abdominal pain, persistent nausea, intermittent vomiting of food and bile and weight loss in the absence of mechanical obstruction (Mathias et al. 1985, Fich et al. 1990). Roux-en Y stasis syndrome has been reported in 10% to 50% of patients after Roux-en-Y gastrojejunostomy (Herrington et al. 1984, Britton et al. 1987). A retrospective review at the Mayo Clinic documented a 30% prevalence of the syndrome after gastric resection, but only 2 (8%) of the 32 patients subjected to total gastrectomy developed stasis symptoms (Gustavsson et al. 1988). Usually early satiety decreases in the course of time, possible due to adaptation of the gut to accommodate a larger volume of food (Hubens et al. 1989).

Since the Roux-en-Y stasis syndrome is thought to result from the jejunal transsection performed during the construction of the Roux-en-Y limb,
an alternative technique, a so called uncut Roux-en-Y, has been introduced by van Stiegmann and Coff (1988). In that operation the small intestine is closed by a stapler without cutting the autonomic nerves. These authors documented excellent gastric emptying in Billroth II patients after this operation, and Miedema and Kelly (1992) found in a canine model that Roux stasis syndrome was prevented by the procedure. Neuromuscular continuity between the proximal jejunum and the Roux-en-Y limb in the stapler line with propagated pacesetter potentials from the duodenal pacemaker to the Roux limb has also been shown to be preserved in dogs (Nguyen-Tu and Kelly 1995). This new uncut Roux-en-Y operation has not yet been performed on humans after total gastrectomy.

**Dumping and diarrhoea**

The term “dumping” was coined by Mix in 1922 in reference to the rapid emptying of gastric content seen on barium radiography in patients with this condition (Eagon et al. 1992). Breakfast, with high carbohydrate liquids is often associated with early postprandial dumping symptoms. Vasomotor and cardiovascular symptoms usually predominate, sometimes without gastrointestinal symptoms. The patient notes rather rapid onset of weakness, faintness, and dizziness and will have an immediate urgent desire to adopt a reclining position. The patient may break out in a cold sweat and is conscious of the heart pounding, she or he may note a feeling of fullness in the epigastrium and a sense of churning in the mid-abdomen. The late postprandial or hypoglycaemic dumping syndrome is much less common (Woodward and Hocking 1987).

After total gastrectomy the primary mechanisms leading to dumping are obvious: lost reservoir function of the stomach and rapid emptying of hyperosmolar carbohydrates into the small intestine. However, after total
gastrectomy not every patient suffers from dumping; the disorder has been reported to occur in 29% of cases (Gustavsson et al. 1988). The most popular theory on the pathogenesis of dumping is the hyperosmolar load theory, according to which rapid passage of hyperosmolar meal to the small intestine results in a marked shift of the extracellular fluid into the lumen (Geer et al. 1990). This results in hypovolaemia and haemoconcentration and dumping symptoms early after the meal. Late dumping is associated with hypoglycaemia, and insulinotropic factors from the small intestine have been proposed to be involved in the pathogenesis. It has been proposed that exaggerated plasma levels of immunoreactive glucagon is due to the abnormal exposure of the distal intestinal mucosa (where the glucagon gene is expressed) to unabsorbed nutrients (Miholic et al. 1991).

All types of gastric surgery may result in diarrhoea postoperatively, but the incidence has been higher in patients who have undergone vagotomy; truncal vagotomy is associated with the highest incidence of postoperative diarrhoea, around 20% (Storer 1976).

**Malnutrition**

Malnutrition has been regarded as a common problem after total gastrectomy (Adams 1967). Some authors have suggested that malabsorption is responsible for postoperative malnutrition after total gastrectomy (MacDonald 1947, Brain 1951), whereas others hold the major cause to be inadequate caloric intake (Kelly et al. 1954, Adams 1967, Bradley 1975). These latter authors have advocated the construction of a gastric substitute to replace the reservoir function of the removed stomach and so to improve the nutrition of the patient. However, post-gastrectomy malnutrition would appear to be a multifactorial problem (Brägelman et al. 1996).
**Lost gastric functions**

In the normal stomach, liquids leave the organ more rapidly than solids. The fundus plays a key role in gastric emptying for liquids, whereas the emptying rate for digestible solids is more dependent on antral motor activity (Chaundhuri and Fink 1991). As the solids reach the distal stomach, they are first ground to 2.0 mm size or less in an acid-peptic medium, while the terminal antrum and pylorus remain closed, then released through the pylorus after mechanical and acid-peptic action has given digestible solids a satisfactory size and chymous-like consistency. The chemical and physical characteristics of gastric contents influence the speed of gastric emptying. After total gastrectomy, over and above the lost reservoir function of stomach, the mixing and the step-by-step delivering of chyme to the small intestine may be impaired. In addition, by Roux-en-Y reconstruction the duodenum is bypassed and the output and mixing of bile and pancreatic enzymes with ingested food is delayed beyond the time necessary for proper digestion (Olbe and Lundell 1987).

In 1907 Moynihan reported a case of total gastrectomy for leather-bottle stomach in a 43 year-old man who survived the cancer but died 3 years later of pernicious anaemia (Moynihan 1907). Intrinsic factor, which is delivered from the parietal cells of the stomach, is necessary for the absorption of vitamin B12 and thereby vitamin B12 substitution is necessary after total gastrectomy. Cristallo’s group (1986) found that low vitamin B12 levels after total gastrectomy were common after the twentieth postoperative month. In seven of the 20 patients after total gastrectomy studied by Bae and associates (1998) vitamin B12 absorption was abnormal. No decreases in serum transferrin, iron levels or total-iron-binding capacity were seen and postoperative anaemia occasionally seen (Bae et al. 1998). Cristallo and colleagues (1986) found that after total gastrectomy serum iron levels were initially low and returned to normal in six months after the operation. Patients
without stomach do not naturally secrete gastric acid any more, and this may, together with altered motility, result in bacterial overgrowth in the upper intestine.

**Weight loss**

Malnutrition and weight loss occurs in most patients after total gastrectomy (Adams 1967). In ten patients studied by Bradley and colleagues (1975) the average weight loss was 25 kg. However, most of the weight loss occurred prior to total gastrectomy. Sategna-Guidetti and Bianco (1989) observed over 10 per cent weight loss in 66 per cent of patients within the first year after total gastrectomy. In a series of 174 patients, Brägelmann’s group (1996) noted that 96% of the patients had lost weight preoperatively and 67% after the operation. Patients with a body mass index below 20 suffered significantly more often from symptoms. At a mean of 4.6 years after operation in patients with total gastrectomy with loop oesphagojejunostomy the average body weight was 15% less than the preoperative weight (Bae et al. 1998). Significant weight loss after total gastrectomy has been recorded by many other observers (Everson 1952, Kelly et al. 1954, Moreno 1956, Huguier 1976, Braga et al. 1988), but both the frequency of weight loss and opinions as to the cause of postoperative malnutrition have been controversial. Contrary to most other reports, Cristallo and associates (1986) did not found weight loss in patients studied one to three years after total gastrectomy with Roux-en-Y reconstruction and concluded that malnutrition is uncommon if an adequate dietary intake is maintained.

**Decreased food intake**

Bradley (1975) has shown that when the patients are under controlled hospital conditions after total gastrectomy, they can take in a well-balanced diet
sufficient in carbohydrates, fats, proteins, vitamins and minerals to maintain proper nutrition. Total caloric intake, as well as the specific intake of carbohydrate, fat and protein, exceeded the Recommended Dietary Allowances (RDA) for sex and age and the patients were physiologically capable of caloric intake adequate to result in weight gain. Food intake decreased significantly when the patients returned to their home environment. Also Braga and colleagues (1988) claimed that malnutrition would not appear to be an inevitable consequence of total gastrectomy, and can be prevented by adequate calorie intake (Braga et al. 1988).

A close relationship between dietary intake and postoperative nutritional parameters has been observed and a strict nutritional follow-up of gastrectomised patients has been recommended (Braga et al. 1988). Brägelmann and co-workers (1996) noted surprisingly high calorie intake after total gastrectomy during the period of controlled diet, almost reaching the recommended value of 40 kilocalories/kg body weight. Such findings do not support the conception that weight loss is caused mainly by low intake.

Bae and associates (1998) compared 20 gastric cancer patients after total gastrectomy with normal controls and found an average daily calorie intake of 1586 kcal, which was lower than the normal intake of Korean adults (1838 kcal). The daily excreted amount of faecal fat was significantly increased in the patients (mean, 28.6 g versus 6.9 g). These results suggested that poor oral intake and fat malabsorption following total gastrectomy are the cause of malnutrition and that fat malabsorption may be related to relative pancreatic insufficiency.

Maldigestion and malabsorption

Proper nutrition initially requires the availability of the 5 essential foodstuffs: proteins, fats, carbohydrates, vitamins and minerals. While access to these
nutrients is necessary after total gastrectomy, it is equally important that proper amounts of these foodstuffs be ingested, that digestion and absorption proceed in a normal fashion, and that incorporation and conversion of these foodstuffs into tissue and energy sources occurs.

Fat malabsorption is the most common malabsorptive disorder after total gastrectomy (Walther et al. 1989a, Curran and Hill 1990, Bae et al. 1998). Malabsorption of carbohydrates (Bae et al. 1998) or proteins (Curran and Hill 1990) has not been found to be a significant problem after total gastrectomy. Because of fat malabsorption, also deficiencies in absorption of fat-soluble vitamins (vitamin D, A and E and K) may be possible after total gastrectomy. Especially deficiency of vitamin D together with calcium malabsorption might result in bone disorders in gastrectomised patients.

Zittel and co-workers (1997) found decreased serum 25-(OH) vitamin D and calcium concentration both after gastric resection and after total gastrectomy. Similar result were obtained when pigs after total gastrectomy were studied by the same group (Maier et al. 1997). The overall rate of vertebral fractures and/or osteopenia among gastrectomy patients after gastric surgery (resection or total gastrectomy) was 55%. Bisballe and colleagues (1991) studied 68 postgastrectomy patients and found reduced serum concentrations of calcium, phosphate, and 25-hydroxyvitamin D, while levels of alkaline phosphatase and 1,25 dihydroxyvitamin were high. Serum 25-hydroxyvitamin D, age and the duration of postoperative follow-up were significant determinants of mineralisation defects, and the results also showed the need for vitamin D supplementation and regular control after gastric surgery.

Decreased serum albumin values have been found after gastrectomy (Walther et al. 1989a), but usually serum albumin is normal in gastrectomised patients. Curran and Hill (1990) found normal mean serum albumin and faecal nitrogen values after total gastrectomy, although there was
notable steatorrhoea of a mean 21 g/day. Zittel and co-workers (1997) did not
found differences in serum or total protein levels comparing different surgical
procedures after total gastrectomy or compared with control subjects.
Totally gastrectomised patients have shown lower serum zinc levels compared
with age-matched controls (Sandström et al. 1987). In 18 patients studied by
Bae and associates after total gastrectomy, no decreases in serum transferrin,
iron levels or total iron-binding capacity were seen (Bae et al. 1998).

Mechanisms of maldigestion and malabsorption after total gastrectomy

Pancreatic insufficiency (Büchler et al. 1988, Walther et al. 1989a, Bae et al.
1998) and pancreatico-cibal dyssynchrony (Tabaqchali 1970, Curran and Hill
1990, Armbrecht et al. 1994) may lead to fat malabsorption. Pancreatic
insufficiency might be due to truncal vagotomy, which is always accompanied
total gastrectomy. Truncal vagotomy has been shown to disrupt
enteropancreatic reflexes and to reduce mucosal release of cholecystokinin
(Cullo et al. 1979).

When the duodenal passage is bypassed, like after Roux-en-Y
reconstruction, it may result in decreased pancreatic and bile excretion by
Pancreatico-cibal dyssynchrony (Tabaqchali 1970, Curran and Hill 1990,
Armbrecht et al. 1994) means that the timing of excreting of pancreatic juice
during digestion is too late to be effective for proper absorption of fats.
Inadequate mixing of digestive enzymes with the ingested fat and diminished
micelle formation due to bacterial overgrowth have also been suggested

Lack of gastric lipase is an inevitable consequence of total
gastrectomy and it might effect fat absorption (Carriere 1993). Shortened small-
bowel transit times after total gastrectomy have been described
(Armbrecht et al. 1988, Brägelman et al. 1996) and this may result in inadequate absorption of nutrients.

Changes in villous morphology and hypertrophy of the circular muscular layer of the small bowel after total gastrectomy have been demonstrated in beagle dogs, but there are only few studies concerning the morphology of the small-intestinal villi after total gastrectomy in humans (Starker et al. 1982). A tendency to significant villous atrophy in the small intestine and decreased disaccharidase activity has been shown (Temegai 1990). In contrary, Sategna-Guidetti and Bianco (1989) did not find either morphological or absorptive alterations in the small bowel or abnormal transit time.

**Intestinal dysmotility**

Neural control of gastrointestinal motility involves the extrinsic autonomic nervous systems as well as a complex network of cholinergic and non-cholinergic, non-adrenergic nerves. Surgical interruption of the vagus nerve, which always results from total gastrectomy, may alter the co-ordination of this complex mechanism, and although truncal vagotomy has no dramatic effect on the gastrointestinal motor pattern *per se*, it may cause severe dysmotility when associated with a surgical repositioning of intestinal loops (Altomare et al. 1997).

Emptying of the normal stomach as well as the upper intestine after total gastrectomy has been studied by radiography, isotopic methods and breath tests (Caride et al. 1984, Miholic et al. 1989, Miholic at al. 1991, Heimbucher et al. 1994). All these methods have different modifications, and this methodological inaccuracy may partly explain the conflicting results obtained by different authors. For example, there is no general agreement as to whether total gastrectomy increases or reduces the intestinal transit time. Different parts of the gastrointestinal tract may have different emptying rates,
and different meal consistency and other factors like smoking and exercise may interfere.

Pellegrini and co-workers (1986) observed slower intestinal transit times after total gastrectomy compared with control subjects. Although transit was slower, food was quickly removed from the upper gastrointestinal area. The authors took this to explain why patients could eat meals of normal size and did not recommend the use of an artificial gastric reservoir after total gastrectomy.

Haglund and colleagues (1989) evaluated oesophageal motor function after total gastrectomy by means of fluoroscopy and scintigraphy, and all except one out of 11 patients yielded abnormal findings 12 months after the operation. In nine patients the emptying of the proximal jejunum was considered normal; one had very rapid emptying and one slow.

Miholic and colleagues (1989) measured the emptying of the upper small intestine and small-bowel transit time with a 99mTc-labeled solid test meal in 11 patients with Roux-en-Y reconstruction and in 9 with jejunal interposition. Rapid emptying was associated with dumping symptoms and shorter oro-caecal transit time. The time from peak activity until clearance of 50% of the activity from the area ranged from two to more than 20 minutes, with no significant difference between the two reconstructions.

During recent years manometric techniques have been available in studying patients after total gastrectomy, but the findings are complex and difficult to interpret (Heimbucher et al. 1994). These methodological difficulties render it more difficult to compare possible physiological differences between different reconstructions after total gastrectomy. Bassotti and associates (1990) were probably the first to study the intestinal motility of the Roux limb by manometry after total gastrectomy, and concluded that patients undergoing total gastrectomy and Roux-Orr anastomosis have significant motor
abnormalities in the reconstructed intestinal limb in both fasting and fed condition.

**Bacterial overgrowth**

There are three main factors which prevent the growth and accumulation of enteric bacteria in the upper intestinal lumen in a healthy person: intestinal motility, gastric acid and immunologic or bacteriostatic intestinal secretions (Haboudi and Montgomery 1992). All of these defence mechanisms may be compromised after total gastrectomy. Microbiologic culturing of jejunal secretions obtained by aspiration has been regarded as the standard method of identifying bacterial overgrowth in the stomach or small intestine (Donalson 1964). Non-invasive breath tests have been evaluated as a means to detect bacterial overgrowth and the breath tests currently used include glucose or lactulose breath tests with sensitivity ranging from 70% to 90% and specificity ranging from 40 to 100% (Rhodes et al. 1979, Kerlin and Wong 1988). The normal concentration of organisms in the upper gastrointestinal tract is $< 10^4$ organisms/ml of intestinal contents (Saltzman et al. 1994).

Bacterial overgrowth of the small intestine can result in bacterial overgrowth syndrome, with malabsorption of fat, carbohydrate, protein and micronutrients, and clinical manifestations such as abdominal pain, diarrhoea and malnutrition. Fat malabsorption may be due to bile acid deconjugation and intestinal mucosal damage caused by the overgrowing bacteria (Kirsch 1990). On the other hand, bacterial overgrowth caused by atrophic gastritis or omeprazole treatment has not been associated with clinically significant fat or carbohydrate malabsorption (Saltzman et al. 1994).

Bacterial overgrowth was demonstrated by culturing jejunal juice in patients with achlorhydria and after Bill gastrectomy, in contrast to acid-secreting individuals (Armbrecht et al. 1985). The number of bacteria in the jejunum after total gastrectomy appears to be significantly increased. Anaerobic
counts ranged from $10^5$ to $10^{10}$/cc. Bacteroides, Clostridia, Veillonella and Lactobacilli predominated among the anaerobic flora of the jejunum and yeast, Streptococci and E. coli have also been found (Bradley 1975). Fat malabsorption has been proposed to result in shortened intestinal transit time and small intestinal bacterial overgrowth (Olbe and Lundell 1987, Armbrecht et al. 1988).

**Quality of life after total gastrectomy**

The number of patients surviving after a gastric cancer operation is assumed to increase due to earlier diagnosis (Ovaska et al. 1990, Macintyre and Akoh 1991, Farley et al. 1992), improved surgical techniques (Siewert et al. 1998, Maeta et al. 1999), and adjuvant chemotherapy (Meyer et al. 1993, Lowy et al. 1999, Yu et al. 1998). In consequence, the quality of life and nutritional problems after potentially curative total gastrectomy will be of great clinical importance in the future (Espat and Karpeh 1999) and new instruments for measuring the quality of life have recently been introduced (Eypasch et al. 1995).

There are studies showing better quality of life after subtotal than after total gastrectomy (Korenaga et al. 1992, Davies et al. 1998). In a prospective study of Schmitz and co-workers (1994) patients with interposed pouch reconstruction revealed better quality of life according to Cuschieri’s assessment compared with patients without a pouch. Buhl and colleagues (1995) compared Hunt-Lawrence pouch, simple oesophagojejunostomy and distal subtotal gastrectomy and concluded that in terms of postoperative functional results as well as quality of life, distal gastric resection has no advantage over total gastrectomy with pouch reconstruction. Patients with pouch reconstruction had also more favourable results assessed by questionnaire including 94 questions concerning general physical complaint,
satisfaction with life and psychosocial burden, compared with patients after total gastrectomy with simple Roux-en-Y reconstruction (Roder et al. 1992). Until now there is some evidence that pouch reconstruction might have advantages compared with other reconstructions after total gastrectomy assessed by different methods measuring the quality of life.
POUCH RECONSTRUCTION AFTER TOTAL GASTRECTOMY

Historical experience
Hoffman (1922) performed a small stoma between the two limbs of the jejunal loop after oesophagojejunostomy, but Steinberg (1949) made a wide stoma between the two limbs and described it as a “pantaloon anastomosis”. One purpose of this anastomosis was to create a large “substitute stomach” to allow substantial meals.

Lee (1951) used the right colon to substitute the stomach and anastomosed the terminal ileum to the oesophagus and the colon portion to the duodenum. The aim of this was to prevent reflux of the pouch into the oesophagus by the ileocecal valve. The operation was performed on three patients. Longmire and Beal (1952) operated on two patients by this technique. They abandoned the method because of serious postoperative complications and described seven patients with isolated jejunal segments transposed between the oesophagus and duodenum. This segment functioned like the colon and was less hazardous to transplant. Transverse colon was used for pouch substitution by Gerwig (1962), but he was not satisfied with the results. Pouches have also been used to increase the volume of the small residual stomach (Knox 1965).

Other parts of the colon have also been used for pouch reconstructions after total gastrectomy (Lee 1951, Hunnicut 1952, Moroney 1953, Herrington 1968). Hunnicut advocated transplantation of the terminal ileum and ascending colon in order to create a gastric reservoir after total gastrectomy and reported results in six patients, one of whom survived for over two years. Hunt (1952) reported the results of his 7 patients with a food pouch made of a segment of jejunum. He made a 15-cm-long pouch and the duodenal contents were diverted by an end-to-side Roux-en-Y technique. No leaks were seen at the site of anastomosis and he believed that the pouch
provided facilities for balanced diet, diverted the duodenal contents and lowered the incidence of reflux oesophagitis. In 1952 Longmire reported on his attempt in November 1944 to form a gastric reservoir by longitudinally splitting the complete antimesenteric wall of the jejunum loop (Longmire and Beal 1952). Gangrene and perforation developed at the oesophageal anastomosis on the tenth day after the operation and the patient died. The same investigators reported 7 cases where an isolated approximately 14-inch-long segment of jejunum was interposed between the duodenum and the oesophagus. The rationale for this Longmire and Beal reconstruction was the assumption that if ingested material passed through the duodenum it was more physiologic. The conception was based on the clinical impression of Higginson and Clagett (1948), that Schoemaker-Billroth I anastomosis following subtotal gastric resection caused less postprandial distress and less difficulty in gaining and maintaining weight than the Hofmeister-Polya-type anastomosis (Billroth BII).

Functional studies of the pouches

Malnutrition after initial recovery from the operative procedure was a frequent accompaniment of total gastrectomy when simple reconstructive procedures like oesophagojejunostomy or oesophagoduodenostomy were employed. This was in fact the major stimulus for developing other, often more complex, means of reconstruction, these being either an interposed bowel segment or a jejunal reservoir (Lawrence 1996). The initial conception of the mechanism underlining postgastrectomy malnutrition envisaged a deficiency of digestive enzymes, a notion which developed on the basis of the fat malabsorption observed following total gastrectomy.
Scott (1968) was among the first to report on metabolic and clinical consequences of pouch reconstruction after total gastrectomy. In a series of twenty-two patients, with 8 long-term survivors living from 3 to 5 years after the operation, most ate only three meals a day and normal quantities of food could be ingested by each. The weight gain was good except in one case, coefficients of fat absorption ranged from 78 to 98 per cent, serum carotene and cholesterol were within normal range, d-xylose tolerance test was normal in seven, serum levels of vitamin A were normal, and only one patient was anaemic. In radiological studies a trend was seen toward a slight dilatation of the jejunal pouch through the years, and two patients showed hiatal herniation of a portion of the pouch. Fluoroscopic study showed good reservoir function in all, without obstruction or undesirable delay in emptying. Two patients developed recurrent bouts of pneumonitis, which necessitated subsequent thoracotomy because of lung abscess in one and to rule out neoplasm in the other.

Bradley and colleagues (1975) evaluated seven patients with Hunt-Lawrence pouch and compared them retrospectively with three patients with simple Roux-en-Y reconstruction. They concluded that jejunal pouch did not favourably affect caloric intake, weight gain, degree of malabsorption or dumping symptoms, and concluded that although some degree of malnutrition does result from total gastric resection, it is in most cases mild and potentially amenable to correction, and that total gastrectomy should not be avoided for fear of postoperative malnutrition. Huguier and co-workers (1976) reported the functional results of 181 patients including six different reconstructive procedures, and among these 3 “neogastrium”, a Hunt-Lawrence pouch.
According to Huguier the best functional results after total gastrectomy were obtained by Roux-en-Y anastomosis and the Henley reconstruction (Henley 1952), which is an isoperistaltic isolated jejunal loop interposed between oesophagus and duodenum.

In cine fluorographic studies by Lygidakis (1981), the Lawrence type reconstruction revealed a marked delay in emptying time of some 4 to 5 hours and barium was shown to regurgitate into the oesophagus in six of the 10 patients treated, together with pouch dilatation and jejunal mucosal thickening. Six out of the 10 patients showed bile reflux into the oesophagus within a year of surgery and 3 of these had oesophagitis. Lykidakis introduced a new reconstruction technique after total gastrectomy, in which a long Roux-en-Y limb is folded upon itself and two anastomoses of 4 cm length are created between the folded jejunum. This new method appeared to give the best functional results in the study in question.

Heartburn has been observed to be more common in patients with long pouch compared with short after jejunal pouch reconstruction (Tanaka et al. 1997).

Motility of the Roux-en-Y limb after total gastrectomy and Roux-en-Y reconstruction with and without a Hunt-Lawrence pouch was compared with that in normal subjects by Thomas and associates (1996) using a manometric technique. Patients treated with Roux-en-Y oesophagojejunostomy without a pouch had an increased number of phases of interdigestive motor complex per hour and the phases were of shorter duration. In patients with a pouch, no differences were detected between the motility in the pouch and that in the efferent limb. The authors concluded that a pouch reduces the overall activity,
which may contribute to the storage function of the pouch. In a previous study
(Heimbucher et al. 1994) the same group tried to describe the motility patterns
of the Hunt-Lawrence pouch and jejunal limb in asymptomatic patients after
total gastrectomy and to determine, whether symptoms after gastrectomy were
related to disturbed motility in the pouch and/or jejunal limb. The altered motility
and reduction in overall activity occurred after a Hunt-Lawrence pouch
reconstruction in asymptomatic patients. No difference was observed between
the motility patterns in the pouch and the jejunal limb. This suggested that the
longitudinal incision required to construct the pouch from the jejunum did not
contribute to additional alterations in the motility of the isolated jejunal segment,
and that the pouch thus is able to contract similarly to the normal jejunum. Four
of the 5 symptomatic patients showed highly abnormal motility with hypomotile
or obstructive pattern.

Herrington (1968) reported on four patients with interposition of
an antiperistaltic segment of the transverse colon between the distal
oesophagus and the duodenum. Each patient lost weight and had symptoms of
reflux oesophagitis. Regurgitation was a prominent feature during the
postoperative follow-up in all of them. Each of the additional five patients with
jejunal interposition was able to eat normal sized meal and none experienced
symptoms of reflux oesophagitis. Among six patients after Hunt-Lawrence
pouch reconstruction weight gain was significant and all were free of
postprandial distress and ate normal-size meals. Emptying time from pouch to
right colon varied from 2 to 4 hours as studied by barium.
Prospective randomized trials

Troidl and associates (1987) performed the first prospective, randomized study comparing two different reconstruction methods after total gastrectomy. They assessed the Hunt-Lawrence pouch with oesophagojejunostomy plus enteroanastomosis, because in a pilot trial they had found no advantage of the duodenal passage of the Longmire-Gütgemann interposition. The trial involved 38 patients (20 pouch and 18 oesophagojejunostomy patients). Patients with the pouch had significantly better survival, they tended to have fewer complications, and the quality of life (appetite, hunger, food intake) favoured this mode of reconstruction. The authors concluded that patients dying within the first year after total gastrectomy suffered an irreversible loss of quality of life and derived no objective benefit from the operation. However, in that study only 39% of the patients survived for at least one year after the operation, and information on the possible long-term benefit of pouch reconstruction was thus limited. Another objection to comparison of this kind of reconstruction was raised by the fact that it might be impossible to distinguish between the effect of Roux-en-Y reconstruction *per se* and the of pouch, because the other group had no division of the small intestine (Lawrence 1996).

Nakane and colleagues (1995) compared three reconstructions after total gastrectomy in a randomized trial: pouch/Roux-en-Y, interpositioned pouch, and simple Roux-en-Y, each group including 10 patients. Patients with pouch and Roux-en-Y reconstruction achieved significantly greater food intake per meal than patients in the other two groups and greater weight recovery than patients with interpositioned pouch. A gastric emptying test revealed satisfactory retention capacity and emptying time of the gastric substitute in the
pouch/Roux-en-Y group. It was concluded that pouch with a Roux-en-Y reconstruction is the most useful of these three procedures in improving the postoperative quality of life. Even though the duodenal passage is a physiologic route, the clinical rating was rather poor in patients with pouch and interposition.

Despite the theoretical superiority of the interposition method, which preserves duodenal passage, as a more physiologic route (Micholic et al. 1990), most surgeons prefer the Roux-en-Y reconstruction as being technically easier. However, no controlled comparison of the two methods with pouch reconstruction was conducted until 1995 (Fuchs et al. 1995): a German two centre study comparing 53 patients with pouch/Roux-en-Y with 53 with pouch/interposition. Neither postoperative complication rate nor survival rate differed between the groups. There was no difference in quality of life between the reconstruction groups according to Visick scoring or Spizer index in patients with 3-year survival and without recurrence. Few patients without recurrence suffered from functional gastrointestinal problems after either of the two reconstructions. Oesophagitis due to entero-oesophageal reflux occurred only in three cases. Thus, the duodenal passage did not appear to be as important as the authors had presumed. However, these results are in contrast with data obtained by Nakane and group (1995) favouring Roux-en-Y anastomosis over duodenal passage.
POSTOPERATIVE NUTRITIONAL SUPPORT AND SUPPLEMENTARY TREATMENT

Early enteral feeding decreases fat oxidation and whole body protein catabolism and improves net nitrogen balance and may decrease postoperative morbidity and mortality in upper GI cancer patients (Hochwald et al. 1997). Enteral nasojejunal feeding has been shown to be safe and well tolerated after total gastrectomy (Sand et al. 1997). Cyclic, nocturnal enteral nutrition has been considered safe, effective and durable treatment for undernutrition in gastrectomised patients (Hébuterne et al. 1999). Branched-chain-enriched amino acid solution improved metabolism and maintained good nitrogen retention without increasing side effects compared with a conventional amino acid solution after total or subtotal gastrectomy (Okada et al. 1988).

Erytromycin has been shown to improve gastrointestinal transit and motility after subtotal but probably not after total gastrectomy (Altomare et al. 1997). The long-acting somatostatin analogue, octreotide acetate, was effective in preventing severe dumping symptoms after gastric surgery (Geer et al. 1990).

Enzyme supplementation has been reported to result in a symptomatic improvement in patients after total gastrectomy, and a small but significant improvement in fat assimilation in patients with moderate steatorrhea (<28 g/day), together with a lower caloric demand to maintain body weight (Brägelmann et al. 1995). Severe primary exocrine pancreatic insufficiency with decreased gastrin, decreased late postprandial pancreatic polypeptide, and increased levels of cholecystokinin was found in 15 patients
three months after total gastrectomy by Friess and colleagues (1996), and pancreatic enzyme therapy was recommended. Also Armbrecht and co-workers (1988) found beneficial effect of pancreatic enzymes on postgastrectomy steatorrhoea. Brägelmann (1999) could not confirm these findings. Calcium and vitamin D substitution therapy after gastrectomy has been recommended by several authors (Alhava 1975, Bisballe et al. 1991, Zittel et al. 1999).

Surgeons often recommend small, frequent meals after total gastrectomy. Carbohydrate rich liquids should be avoided and solids should be eaten separately. Harju and Nordback (1987) suggested that guar gum gives a possibility to avoid symptoms related to large volume or high glucose content of a meal. Dietary short chain fructo-oligosaccharides increased iron absorption and prevented completely postgastrectomy anaemia in rats after total gastrectomy (Ohta et al. 1999).

Although absorption of vitamin B12 substitution has been abnormal in 64% of patients after total gastrectomy (Bae et al. 1998), there are surprisingly few data on the optimal dosage and interval of dosages of B12 vitamin substitution therapy after total gastrectomy (Cristallo et al. 1986). Cristallo’s group studied nutritional status and the prevalence of malabsorption in 12 patients one to three years after total gastrectomy. Low vitamin B12 levels were common after the twentieth postoperative month, while serum iron levels were initially low and returned to normal six months after the operation.
AIMS OF THE PRESENT STUDY

The study addressed the following issues:

1. Is the morbidity or mortality rate increased in pouch reconstruction after total gastrectomy compared with Roux-en-Y reconstruction?

2. Does pouch reconstruction diminish postoperative symptoms? Does this possibly occur early in the postoperative course or later after the operation?

3. What are the emptying properties of the upper intestine after total gastrectomy and pouch reconstruction? Is there a difference between solids and liquids?

4. What is the effect of pouch reconstruction on the bacteriology of the upper intestine?

5. Does pouch reconstruction increase patients’ eating capacity?

6. What is the effect of pouch reconstruction on postoperative weight and nutrition?

7. What are the long-term consequences of pouch reconstruction?
PATIENTS AND FOLLOW-UP

Study I
All patients who had histology-proven gastric malignancy and underwent total gastrectomy in Tampere University Hospital between March 1988 and October 1992 were originally considered for the study. Only those with potentially curative total gastrectomy were included. Metastases were preoperatively excluded by clinical examination, chest radiography, abdominal ultrasonography and operative abdominal exploration. Fifty-three subjects were initially included. Four were excluded from study I after the operation, because the final histology demonstrated minimal liver metastases in 2 and the gastric tumour to be lymphoma instead of carcinoma in 2. The postoperative chemotherapy in these two patients could have affected the follow-up parameters in that study.

Study II
Forty-six of the randomized patients were alive and available for a lactulose breath test at least 6 months after total gastrectomy; 22 in the Roux-en-Y group and 24 in the pouch group. Forty-three patients were available for the glucose breath test; 21 Roux-en-Y and 22 pouch.

Study III
A scintigraphic emptying test was performed on forty-five patients: 21 with a simple Roux-en-Y reconstruction (Roux-en-Y group) and 24 with a pouch in the Roux-en-Y segment (pouch group). The test was applied at mean of 15 months after the operation.
Study IV

Patients surviving at least 3 years after total gastrectomy

The long-term follow-up study population comprised those randomized 32 patients with gastric carcinoma and 2 patients with gastric lymphoma who were alive without residual tumour at least 3 years after the operation (pouch group, n=20; Roux-en-Y group, n=14). Two of these patients with gastric lymphoma had been excluded from study I.

All patients were followed up at the outpatient clinic in Tampere University Hospital at three-month intervals until two years by the primary investigator and thereafter at six-month intervals until five years by the GI surgeons. After five years, if the condition of the patient was stable, follow-up was arranged yearly by the family doctor and information during that time obtained from the medical records and personal communication with the family doctors. The mean follow-up in the pouch group was 6.9 years (range 3.6 - 9.4 years) and 7.1 years (range 4.0 - 9.2 years) in the Roux-en-Y group.

Long-term survivors

Twenty-six patients were still alive in February 1999 (12 in the pouch group and 14 in the Roux-en-Y group) and a standard questionnaire (Appendix) was mailed to all. Nine patients in the pouch group (75%) and twelve in the Roux-en-Y group (86%) responded. One patient in the pouch group had moved abroad and could not be reached.
METHODS

Operation and randomization (I)
The indication for total gastrectomy was 1) a proximal upper-third gastric
tumour or 2) a distal gastric tumour when the carcinoma was of diffuse type
according to the classification of Lauren (Laurén 1965). In 18 patients the
tumour was located in the cardia or fundus and in 24 patients carcinoma was
diffuse type. Total gastrectomy together with extended D 2 lymphadenectomy
was performed, with plenectomy only when the tumour was located in the
greater curvature against the spleen. A small resection of the tail of the
pancreas was made in 2 patients with suspected tumour infiltration.
Cholecystectomy was undertaken only when gallstones had been detected in
preoperative ultrasound or at operation.

After radical gastrectomy and D2 lymphadenectomy the patients
were randomized according to the sealed-envelope method either to the jejunal
pouch reconstruction group (pouch group) or to Roux-en-Y group (control
group). In all patients the jejunum was divided with a stapler 30 cm below the
ligament of Treitz. In the pouch group a 15-cm-long jejunal pouch (Fig. 3) was
made with linear staplers (GIA, US Surgical Corporation, or
PLC, Ethicon®).

In pouch patients the intraluminal stapler line and the pouch stapler
line were contiguous and positioned at a 90-degree angle to avoid
compromising the circulation. Anastomotic integrity was checked under saline
by air insufflation through a naso-oesophageal tube. The Roux-en-Y end-to-
side anastomosis was made 50 cm distally from the oesophagojejunal
anastomosis. In the control group the reconstruction was identical except a
jejunal pouch that was not created. In the control group the oesophagojejunal
end-to-side anastomosis was made 2 cm from the division of the jejunum.
The duration of the operation and intraoperative blood loss were recorded. Total parenteral nutrition via the central venous line was used for five days unless complications required prolongation. The anastomosis was checked on day five by a swallow of contrast medium and enteral feeding was started unless leakage was observed. Leakage was considered clinically significant when radiological leakage was accompanied by fever and leukocytosis. The postoperative complications and hospital stay were recorded.

The study protocol was approved by the ethics committee of Tampere University Hospital, and informed consent was obtained from each patient.

Figure 3. Jejunal pouch reconstruction
Evaluation of symptoms and survival (I, IV)

After discharge from hospital the patients were seen at the outpatient clinic commencing one month after the operation at three-month intervals until one year, and six-month intervals until two years. Information on further survival in study I was obtained by personal communications. A standard questionnaire (Appendix) was used to determine the occurrence and the subjective severity of dumping symptoms (postprandial faintness, sweating, nausea), early satiety, regurgitation and dysphagia on a scale from 0-3 (no, mild, moderate, severe). In addition, diarrhoea was determined on a scale of 0-2, where 0 was no diarrhoea, 1 was two to four loose stools a day and 2 more than four loose stools a day or need for antidiarrhoeal medication.

Height and body weight were measured during the follow-up to calculate the body mass index (BMI).

A standard questionnaire (Appendix) similar to that used in the outpatient clinic during 2-year follow-up was mailed to all patients living still in February 1999. In addition to symptoms and eating capacity, appetite, weight, and the latest haemoglobin concentration were obtained as were the number of daily meals and snacks. Appetite was scored as good, moderate or no appetite.

Test meal and evaluation of eating capacity (I, IV)

At six months after a 12-hour fast the patients consumed a standard 520 kcal test meal weighing 640 g, and consisting of meat, potato, bread, green salad, and milk. After consumption the remainder of the meal was weighed to measure the patient’s eating capacity.

The patients were requested to estimate the size of the meal they were able to eat compared with the amount they ate preoperatively. Normal preoperative meal size was regarded as 100% and postoperative eating capacity was expressed as a percentage of the preoperative amount.
Lactulose breath test (II)

The lactulose breath test was used to determine the mouth-to-caecum transit time (MCTT) (Ladas et al. 1989), and was performed 15 months after the operation. The test was performed in the morning and patients fasted overnight (12 hours) and during the test. They were not allowed to participate in any physical activity sufficient to produce hyperventilation and were not allowed to smoke throughout the breath test study. Antimicrobial therapy was not permitted for one month before the study. Breath hydrogen (H₂) and methane (CH₄) determinations were made on end-expiratory breath specimens. Samples were analysed for hydrogen and methane concentrations with a gas chromatograph. The results were expressed in parts per million (ppm). The respective tests were performed on separate days.

In the lactulose test 20 g/30 ml of lactulose syrup (Levolac®) was given as a bolus after basal fasting specimen determination. Post-dosing breath H₂ and CH₄ determinations were performed every ten minutes for one hour and thereafter every 15 minutes for four hours or until a peak in the concentrations was detected. The first peak during the test was regarded as bacterial overgrowth of the small intestine and the second was used for transit time calculation. The MCTT was defined as the time at which a sustained increase in breath hydrogen (or CH₄ in "non-H₂-producers") concentration (ppm) was noted in three consecutive samples, where at least a 10-ppm incremental increase appeared between any two of the samples (Caride et al. 1984).
Glucose breath test (II)

The tests were performed after at least six months postoperatively, this time being considered the minimum for adaptation and recovery from the operation. In the glucose breath test 50 g glucose in 250 ml of water was given and post-dosing breath hydrogen and methane determinations were made every 10 minutes for two hours. A rise in breath H$_2$ or CH$_4$ concentration of at least 12 ppm over the baseline was considered positive for bacterial overgrowth in the upper small intestine if this appeared before the caecal (second) peak in the lactulose test (Kerlin and Wong 1988).

The patients were considered "non-H$_2$-producers" or "non-CH$_4$-producers" if they failed to generate detectable breath H$_2$ or CH$_4$ within two hours. The minimum concentration for H$_2$ was set at 20 ppm and for CH$_4$ 2 ppm (Cloarec et al. 1990). The maximal concentration of breath hydrogen or methane and the time when the maximal peak appeared was determined in both breath tests. The concentration of breath hydrogen or methane was expressed by parts per million (ppm).

Scintigraphic emptying test (III)

The emptying rate of the upper jejunal Roux-en-Y segment or the pouch was assessed by a $^{99m}$Tc-Technetium-labelled solid test meal. The scintigraphic emptying test was done after a 12-hour fast. Any medical therapy which could possibly have influenced the test was discontinued. A solid test meal was prepared by mixing 20 MBq $^{99m}$Tc-Hepatate® (Amersham International PLC, Buckinghamshire, England) with a 20 g raw egg; 50 g of raw minced meat was gradually mixed with the labelled egg; 10 g of wheat flour and 2 g of salt was added and the burger baked in a microwave oven for two minutes (Kerrigan et al. 1989). The meal was served with 50 ml water, and the radioactivity was measured with the patient semisupine. The recording was made dynamically.
between 0-30 minutes and thereafter at 15-minute intervals for three hours. In
the analysis three regions of interest were drawn, the first over the pouch or the
upper jejunal area, the second over the lower intestine, and the third (for background) beside these. A special computer program was designed to
combine dynamic and the static recordings. A time-activity curve was then
produced for a pouch or upper jejunal area after a decay correction for the
physical half-life of $^{99m}$Tc and background subtraction. The relative activity at
three hours was used as a measure of the emptying rate.

**Blood biochemistry (I, IV)**

Blood haemoglobin concentration, serum albumin, transferrin, iron, calcium,
potassium, sodium, magnesium and 25-(OH) vitamin D concentrations and
serum alkaline phosphatase (ALP) and alanine aminotransferase (ALAT)
activities were determined at 6-month intervals up to 2 years and at 3 years or
more postoperatively. B12 vitamin and folate concentrations were recorded at
6-month intervals until 2 years.

**Endoscopy and histology (I, IV)**

Upper endoscopy with biopsy of the jejunal loop, pouch when present, and
oesophagus was carried out three months, 12, 24 and at least 36 months after
the operation to detect possible endoscopic or histologic inflammation in the
pouch or jejunum or in the oesophageal mucosa.

**Statistics**

The results were expressed as mean values±SD or as mean values and range.
Chi-square test, Mann-Whitney U-test, Student’s t-test and Fisher’s exact test
were used to assess the significance of differences, and probabilities of less
than 0.05 were accepted as significant.
RESULTS

Primary results of the pouch operation (I)

Mean operation time was 197 (range, 120-330) minutes in the pouch group and 195 (range, 140-250) minutes in the control group (NS). Mean intraoperative blood loss was 697 (range, 250-2000) ml in the pouch group and 777 (range, 250-1700) ml in the control group (NS). There was no hospital or 30-day mortality. 17 (65%) patients in the pouch group and 8 (35%) in the control group developed complications (p=0.03). The most frequent complications were intra-abdominal infection, pneumonia and leakage in the oesophagojejunal anastomosis. The overall leakage rate (including all suspicious cases in routine postoperative swallow of contrast medium) was increased in the pouch group compared to the control group (30 % vs. 4 %, p=0.03). This difference disappeared when the two subclinical radiological leakages were excluded. The two patients in question recovered without fever, leukosytosis or intra-abdominal infection. Other complications and the need for reoperations did not differ between the study groups. The patients in the pouch group had on an average 7 days longer mean hospital stay (19 days vs. 12 days, p=0.02). During the two years follow-up 10 patients died: 6 from metastatic carcinoma and 4 from unrelated reasons. There were no difference in survival between the groups.

Symptoms

Two-year follow-up (I)

Overall 38 % of the patients suffered from dumping postoperatively. Dumping was less frequent in the pouch group at 6, 9, 18 and 24 months postoperatively than in the control group (Figure 4a). The occurrence of dumping decreased in the pouch group but not in the control group during the 2-year follow-up period. Early satiety was significantly more common in the control group at 3 and 18
months after the operation (Figure 4b). At three months dysphagia was more common in the control group (17% vs. 55%, \(p=0.01\)). There were only minor differences between the groups in the occurrence of diarrhoea and regurgitation. Dumping and early satiety were more intensive at most-time points in the control group than in the pouch group and at three months dysphagia was likewise more intensive in the controls (score 1.1, SD 1.2 vs. 0.3, SD 0.7, Mann-Whitney U-test, \(p = 0.001\)).

Figure 4. Dumping and early satiety in the pouch group and in the control group during the two-year follow-up. a. occurrence of dumping. b. occurrence of early satiety (* \(p<0.05\), chi-square test).
Patients surviving at least 3 years after total gastrectomy (IV)

Dumping was more frequent in the control group than in the pouch group at three months and at 2 and 3 years postoperatively (Figure 5a). Early satiety occurred more often in the control group at 3 months and at 1 and 3 years postoperatively (Figure 5b). Dysphagia occurred in 9 (64%) patients in the control group and 4 (20%) in the pouch group at 3 months (p<0.05) (Table V). There was no difference between the groups in the occurrence of diarrhoea or regurgitation.
Table V. Occurrence of postoperative symptoms at different time points during the follow-up. Number of symptomatic patients (%).

<table>
<thead>
<tr>
<th></th>
<th>Roux-en-Y (n=14)</th>
<th>Pouch (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=12 at 8 years)</td>
<td>(n=9 at 8 years)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>9 (64)</td>
<td>4 (20) *</td>
</tr>
<tr>
<td>1 year</td>
<td>5 (36)</td>
<td>2 (10) p=0.108</td>
</tr>
<tr>
<td>2 years</td>
<td>2 (14)</td>
<td>3 (15) p=0.558</td>
</tr>
<tr>
<td>≥3 years</td>
<td>5 (36)</td>
<td>1 (5) p=0.141</td>
</tr>
<tr>
<td>8 years</td>
<td>7 (58)</td>
<td>2 (22) p=0.221</td>
</tr>
<tr>
<td>Regurgitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>5 (36)</td>
<td>5 (25) p=0.498</td>
</tr>
<tr>
<td>1 year</td>
<td>5 (36)</td>
<td>3 (15) p=0.277</td>
</tr>
<tr>
<td>2 years</td>
<td>4 (29)</td>
<td>5 (25) p=0.802</td>
</tr>
<tr>
<td>≥3 years</td>
<td>4 (29)</td>
<td>5 (25) p=0.802</td>
</tr>
<tr>
<td>8 years</td>
<td>8 (67)</td>
<td>5 (56) p=0.687</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>3 (21)</td>
<td>4 (20) p=0.170</td>
</tr>
<tr>
<td>1 year</td>
<td>1 (7)</td>
<td>2 (10) p=1.000</td>
</tr>
<tr>
<td>2 years</td>
<td>1 (7)</td>
<td>1 (5) p=1.000</td>
</tr>
<tr>
<td>≥3 years</td>
<td>3 (21)</td>
<td>2 (10) p=0.628</td>
</tr>
<tr>
<td>8 years</td>
<td>3 (25)</td>
<td>) p=0.228</td>
</tr>
</tbody>
</table>

* p<0.05, Fisher’s exact test.

Long-term survivors (IV)

Dumping, early satiety, dysphagia, regurgitation, and diarrhoea tended to be commoner in the control group than in the pouch group but without statistically significant difference (Figure 5a and 5b, Table V). In one patient in the pouch group with moderate regurgitation symptoms a partial hiatal herniation of the pouch was seen in the oesophagogastric radiograph. Another patient in this group suffered from coeliac disease, which was misdiagnosed, and she occasionally suffered vomiting and hyponatraemia. An 80 year-old woman
suffered from colitis and had attacks of unconsciousness, probably because of hypoglycaemic disturbances. One patient in both groups suffered from unexplained fever, which appeared mostly after physical exercise. Three patients in the pouch group developed urticaria reaction during the follow-up; one developed dermatitis herpetiformis, cured by gluten-free diet, and one had angioneurotic oedema. One patient in the Roux-en-Y group had dermatological symptoms (erythema nodosum).

**Eating capacity**

**Two-year follow-up (I)**

The pouch group patients reported retained ability to eat close to full meals throughout the two-year follow-up (Figure 6). The control group patients experienced a decreased ability to eat compared to those in the pouch group. This eating disability improved during the two-year follow-up (Figure 6). The standard test meal six months after gastrectomy demonstrated greater eating capacity in the pouch group than in the controls (501±236 g vs. 372±222 g, p< 0.001).

**Figure 6.** The reported eating capacity in the pouch group and in the control group during the 2-year follow-up period. The preoperative eating capacity is marked 100%. Mean values±SD are shown. * p < 0.05, Mann-Whitney U test; † p< 0.05 (paired t-test).
Patients surviving at least 3 years after total gastrectomy (IV)
Eating capacity was better in the pouch group than in the control group throughout the 3-year follow-up (Figure 7). In the control group eating capacity seemed to improve steadily during the 3 years. The mean number of daily consumed meals (all kinds of meals) at least 3 years postoperatively was 5.3 (range, 3-7) in the control group as against 2.7 (range, 1-5) in the pouch group (p<0.05).

Long-term survivors (IV)
Eight years after total gastrectomy the mean number of daily meals was 1.8 in the pouch group and 3.9 in the Roux-en-Y group, and the mean number of daily snacks 2.9 in the pouch group and 3.9 in the Roux-en-Y group, without significant difference between the groups. The appetite was good in 7 out of nine (78%) patients in the pouch group and in 7 out of twelve (58%) in the Roux-en-Y (NS).
**Nutrition and postoperative weight loss**

**Two-year follow-up (I)**

BMI decreased from the preoperative level by about two units during the first three months, without further changes and without differences between the study groups (Figure 8). The proportion of patients with BMI less than 19, considered the lower normal range (Cronk and Roche 1982), varied between 8% and 20% at different time points during the two-year follow-up, without difference between the groups or tendency to significant change during the follow-up.

**Figure 8.** BMI (eight in kg/height² in m) in the pouch group and in the control group. Mean values and ±SD are shown. BMI decreased significantly in both groups during the first 3 postoperative months. * p < 0.01, paired t-test.
Patients surviving at least 3 years after total gastrectomy (IV)
The mean postoperative weight loss at three years was 9.9 kg (range from -24 kg to ±0 kg) in the Roux-en-Y and 1.5 kg (range from -6 kg to +5 kg) in the pouch group (p < 0.05). In both groups weight loss was most marked during the first 3 months after the operation. The patients in the pouch group reached almost their preoperative weight at 3 years, whereas the weight of the patients in the control group did not increase during the 3-years follow-up period (Figure 9).

Figure 9. mean postoperative weight loss (kg) during the long-term follow-up in the study groups. At 0.5, and 3 years postoperatively the weight loss was significantly greater in the Roux-en-Y group (p < 0.05, Mann-Whitney U-test).
Blood haemoglobin, serum albumin, iron, transferrin, calcium, potassium, sodium or magnesium concentrations did not differ between the study groups at any observation time during the follow-up period and the values were mostly within normal range. In the control group mean serum alkaline phosphatase activity increased during the 3 years from preoperative mean level of 163 U/l to 248 U/l at 3 years (p<0.01) and tended to be higher than in the pouch group 3 years after the operation (mean 248 U/l in the control group vs. mean 216 U/l in the pouch group, NS). 25 (OH) vitamin D concentration tended to be higher in the pouch group compared with the Roux-en-Y group at 3 years postoperatively (mean 33.9 nmol/l vs. 47.3 nmol/l, NS).

**Emptying of the upper intestine**

**Emptying of solids (III)**

In the solid isotope emptying test activity started to decrease slowly in both groups. In 79% (19 of 24) of the pouch group patients the activity was more than 50% at three hours, whereas in the control group the activity was more than 50% in 43% (9 of 21) of the patients, (p=0.02). The mean (SD) activity at three hours was 82 (±27) % in the pouch group and 44 (±42) % in the Roux-en-Y group (p<0.01) (Figure 10).

**Figure 10.** Time activity curves of the study groups in the scintigraphic emptying test (mean and standard deviation). Mean activity at 3 hours was 82% in the pouch group and 44% in the Roux-en-Y group (p<0.01). • Pouch group (n=24), □ Roux-en-Y group (n=21).
Emptying of liquids (II)

Mean mouth-to-caecum transit time (MCTT) was 110 (range, 30-180) minutes in the control group and 117 (range, 40-210) minutes in the pouch group (NS). In the lactulose breath test six patients were "non-H\textsubscript{2} producers" (maximal H\textsubscript{2} < 20 ppm). In four of these patients MCTT could be determined by the peak in breath \textit{CH}\textsubscript{4} concentration.

There was no association between the mouth-to-caecum transit time and postoperative weight loss or between MCTT and biochemical measurements (blood haemoglobin, serum albumin, iron, calcium and magnesium). The basal and maximal hydrogen and methane concentrations and the time of maximum concentration of H\textsubscript{2} and \textit{CH}\textsubscript{4} did not differ between the study groups.

The MCTT was shorter in patients (n=6) with severe dumping symptoms (60±28 minutes) than in those (n=23) who did not have dumping symptoms (115±41 minutes; p=0.04).

Bacterial overgrowth of the upper intestine (II)

Positive finding in the glucose breath test is presented in Figure 11. In the glucose breath test only eight out of 43 patients examined (four in each group) appeared not to have a pathologic rise in the H\textsubscript{2} concentration (> 12 ppm). Three of them were "non-H\textsubscript{2}-producers", who evidenced an early rise in breath \textit{CH}\textsubscript{4} concentration. Thus, only five out of 43 patients (12\%) after total gastrectomy had normal bacteriological status of the upper gastrointestinal tract and 88 \% had bacterial overgrowth (91 \% in the pouch group and 86\% in the Roux-en-Y group, NS). Furthermore, in one of these negative ("normal") patients the ingested glucose amount was only 10 grams (standard amount 50 grams) because of the fear of symptoms and this may have caused false-negative result.
In the glucose breath test a negative correlation was observed between the maximal hydrogen concentration and postoperative weight loss, serum albumin, and serum iron concentration. Blood haemoglobin concentration tended to be lower in patients with a high maximal hydrogen concentration in the glucose breath test. The correlation was positive between the maximal hydrogen concentration and serum ALP activity.

Figure 11. A typical finding in the glucose breath test. Early increase in the alveolar hydrogen concentration shows bacterial overgrowth in the upper intestine.

Endoscopy and histological findings

Two-year follow-up (I)

Six patients developed anastomotic stricture at the oesophagojejunal junction requiring one or more endoscopic dilatations, 3 in the pouch group and 3 in the control group. Three patients had mild microscopic oesophagitis, all of them in the pouch group (NS). In one patient in each group the jejunal villi demonstrated atrophy. This could be reversed with a gluten-free diet partially in
one patient and totally in the other. No patient evidenced macroscopic or microscopic pouchitis. None of the patients in either group had bezoar formation in the pouch or upper jejunum during the two-year follow-up.

Patients surviving at least 3 years after total gastrectomy (IV)
The upper end of the Roux-en-Y limb was dilated in three patients and one patient in the pouch group developed a bezoar in the pouch 5 years after pouch reconstruction. The bezoar was treated by endoscopy and the symptoms disappeared. None of the study patients showed oesophagitis, inflammation of the Roux-en-Y limb or "pouchitis" in the histological examination. In Figure 12 a radiograph of a pouch is seen five years after the operation.

Figure 12. A radiograph of a pouch five years after total gastrectomy with jejunal pouch reconstruction.
DISCUSSION

Patients
Mean age and other patient characteristics between the study groups were comparable. In the Western countries gastric cancer occurs mainly in elderly patients with many concomitant diseases, and these may effect on the postoperative symptoms and quality of life. Gastric cancer is a quite rare disease and there are only few patients with early stage disease. So it took four years in one big university hospital to collect and randomise 51 patients for this study. The number of patients has been relative small also in other randomised studies. In the study of Nakane and co-workers (1995) comparing 3 different reconstructions after total gastrectomy the number of patients was 10 in one group.

Mortality and morbidity
There was no operative mortality in this study. There was no difference in mortality or carcinoma recurrence rate between the groups. Neither was there a difference in operating time or blood loss between the groups. Thus, reconstruction of the jejunal pouch gives no advantage or disadvantage in these respects.

The total rate of complications was higher in the pouch group than in the controls due to the higher rate of leakages in the oesophagojejunal anastomosis. The clinical leakage rate of 4% in the control group corresponds well with that in previous studies (Inberg et al. 1981, Ovaska et al. 1989), but the clinical anastomotic leakage rate (19%) in the pouch group was higher. Two patients in the pouch group had only radiological leakage in the oesophagojejunal anastomosis but no signs of infection, and they recovered as quickly as the patients without leakage. A possible explanation for the increased leakage rate in the pouch group is that pouch reconstruction may compromise the intestinal wall circulation, resulting in impaired healing of the
anastomosis. A less likely explanation is increased luminal tension in the pouch, because this should have been well enough decompressed by the naso-pouch tube routinely inserted at operation. The complications observed in the pouch group resulted in a longer hospital stay but did not increase mortality. These complications do not necessarily invalidate the operation, but indicate further development of the surgical technique. Furthermore, after this study the stapling technique of the pouch reconstruction was modified, a short rim of intact intestinal wall is left to the upper part of the stapler line, and leakages have since been avoided (unpublished data).

Symptoms
Most authors have found dumping and postprandial epigastric pain (early satiety) to be the most common symptoms after total gastrectomy and Roux-en-Y reconstruction (Olbe and Lundell 1987). Dumping symptoms are typically observed after ingestion of a carbohydrate-rich meal. In our study, dumping occurred during the 2-year and long-term follow-up period in 50 to 65% of patients in the control group, but only in 10% to 25% in the pouch group. In the pouch group the proportion of dumping patients decreased during the two-year follow-up (Fig. 4a). The most popular theory as to the pathogenesis of dumping is the hyperosmolar load theory (Geer et al.1990), according to which the loss of the stomach results in rapid passage of a hyperosmolar meal to the small intestine, with a marked shift of the extracellular fluid into the lumen. This results in hypovolaemia and haemoconcentration. The mechanism whereby jejunal pouch is associated with less dumping remains to be elucidated. One possible explanation is that the pouch might retain some of the ingested food and thus slow the passage as was shown in our pouch patients.

In many patients with a Roux-en-Y reconstruction after total gastrectomy the upper gastrointestinal symptoms diminish during follow-up if the patient has an otherwise favourable clinical course (de Almeida et al.)
However, this was not the finding in a recent study by Nakane and colleagues (1995). In our patients the occurrence of dumping decreased in the pouch group from 30% to 12%, but remained on the level of 50% in the control group during the 2-year follow-up.

A functional obstruction of the Roux limb or "Roux-Y-syndrome", probably due to a defect in the motor function of the limb, has been proposed as a reason for postgastrectomy symptoms such as early satiety, epigastric pain, nausea and vomiting (Eagon 1992). Fifty to eighty per cent of the control group patients in this study reported early satiety. The figures were lower (from 10 to 25%) in the pouch group both during the first two-year follow-up and three years after total gastrectomy among the patients surviving at least three years. A pouch may thus function as a substitute for the gastric reservoir function.

The occurrence of regurgitation, oesophagitis and strictures did not differ between the groups. Thus, pouch reconstruction does not induce symptomatic regurgitation. The lack of acid due to total gastrectomy and the lack of bile reflux due to Roux-en-Y reconstruction may be important reasons for the relatively infrequent occurrence of regurgitation symptoms.

Early after the operation patients reported dysphagia significantly less often in the pouch group than in the control group. One explanation is that early satiety, also less frequent in the pouch group, was reported by the patients as dysphagia symptoms. Endoscopies elicited no explanation for this difference.

**Eating capacity**

Increased eating capacity could be shown in pouch patients compared with the simple Roux-en-Y patients both by the standard questionnaire technique and by the standard test meal study during the first two years of follow-up. A better ability to eat was also found in this group at three years after total gastrectomy,
but eight years postoperatively there was no difference between the groups. This might reflect the fact that the adaptation period is very long after total gastrectomy. The number of daily meals and snacks associates with eating capacity, i.e. those patients who have to eat frequently have lower eating capacity and if they eat more - for example a normal-size portion - they experience early satiety and abdominal pain. This inability to eat normal-size meals seemed to result in increased weight loss after Roux-en-Y reconstruction compared with patients treated with pouch reconstruction.

**Nutrition and postoperative weight loss**

Weight loss is common after total gastrectomy (Bradley et al. 1975). Malabsorption might be one explanation for this (Adams 1967). Of the many possible mechanisms for malnutrition inadequate food intake is perhaps the most important (Olbe and Lundell 1987). BMI decreased by two units in the control group early after the operation, without further change during the follow-up (Figure 8). A pouch seems not to have significant effect on BMI during the two-year follow-up. Also previously the effect of a jejunal pouch on postoperative weight loss has been shown to be temporary (Troidl et al. 1987, Nakane et al. 1995). In the present study the weight loss in the pouch patients tended to be less severe than in the controls, but when BMI values were compared the difference was not significant. However, three years after total gastrectomy the pouch patients had lost significantly less weight than their Roux-en-Y counterparts (mean 1.5 kg vs. 9.9 kg, p<0.05) (Figure 9). This possibly explained the fact that during the two-year follow-up the cancer-related situation affected the results but not the results after three years because patients surviving more than three years were free from cancer.

Since many of the metabolic studies after total gastrectomy have included patients with gastric malignancy, it has been uncertain whether the development of postoperative malnutrition reflects the progression of
malignancy or results from postoperative alterations in the physiology of digestion and absorption.

The untreated coeliac disease in one patient and severe colitis symptoms in another patient before treatment during the follow-up probably influenced the results of the pouch group, as well as the hiatal herniation in one pouch patient.

Emptying of the upper intestine

Emptying of solids

There are few studies on the motility of the jejunum after pouch reconstructions and the results are conflicting (Miholic et al. 1989, Berglund et al. 1991, Heimbucher et al. 1994, Nakane et al. 1995). The mechanism underlying the improvement in symptoms and nutrition after pouch reconstruction might be the reduced intestinal transit time, reduced intraluminal pressure and the reservoir function of a pouch. The lower pressure and increased volume of an S-shaped reservoir compared with the straight Roux-en-Y reconstruction was shown in a recent study (Berglund et al. 1991). In the present series the emptying of the jejunal pouch was slower than that of the straight Roux-en-Y reconstruction. Nevertheless, the delayed emptying did not result in retention of food in the pouch. The likely mechanism by which the pouch reconstruction increases the quality of life after total gastrectomy lies in the reduction of intestinal motility, which contributes to the storage function of the pouch (Berglund et al. 1991, Heimbucher et al. 1994, Thomas et al. 1996).

The emptying of the jejunal segment after total gastrectomy has been studied by Miholic and group (1989) in a small number of patients with either Roux-en-Y or jejunal interposition using granulated resin labelled with 74 mBq $^{99m}$Tc. They found rapid emptying of the upper intestine with a T1/2 of only a few minutes. An association was also seen between rapid emptying and dumping symptoms. The rapid emptying of the upper intestine in that study
may indicate the liquid phase of chyme. In another study by Pellegrini and co-workers (1986) food did not stagnate in the Roux-en-Y limb. The meal in that case consisted of 213 g beef stew and 30 g of chicken liver labelled by subcapsular injection of normal saline solution containing $3.7 \times 10^7$ Bq of $^{99m}$Tc sulphur colloid. The region of interest was the left upper quadrant of the abdomen. Our results are in accordance with those in some other studies (gastric resection with Roux-en-Y reconstruction), where delayed emptying or "Roux-Y syndrome" has been detected (Mathias et al. 1985, Perino et al. 1988). Delayed gastric emptying after a Roux-en-Y reconstruction has also been detected in animal studies and a new type of "uncut Roux" has been advocated (Nguyen-Tu et al. 1995). Hunt-Lawrence pouch motility has been studied with water-perfused manometry by Heimbucher and associates (1994), and altered motility was found in the pouch both after jejunal interposition and after Roux-en-Y type reconstruction, with little correlation between clinical symptoms and clinicophysiological findings.

If the purpose of a gastric substitute is to delay emptying, this was achieved by the jejunal pouch in this study (Figure 10). On the other hand, even the emptying of the simple Roux-en-Y reconstruction was delayed compared with our control series of patients with normal stomach (Viljakka et al. 1999). It may therefore be assumed that the main purpose in creating a pouch is not to delay the emptying of food in the upper intestine, at least not the emptying of solid food. This delayed emptying of the pouch - although it is associated with reduced symptoms and increased food intake - might result in retention with bacterial overgrowth or mucosal lesions of the pouch. However, during the long-term follow-up we observed no such side-effect. Only one patient developed a bezoar in the pouch 5 years after the operation. There is clearly a need for more long-term follow-up studies of pouch reconstruction after total gastrectomy.
Emptying of liquids

In this series mouth-to-caecum transit time was measured by the lactulose breath test, which has been shown to correlate with the isotope method in healthy human volunteers (Caride et al. 1984). We compared the intestinal transit time of liquids after pouch reconstruction with that in a simple Roux-en-Y reconstruction and found no prolongation in the patients with pouch reconstruction compared with Roux-en-Y. There was no association between the transit time and nutritional parameters (biochemical, postoperative weight gain). Only severe dumping symptoms were associated with shortened transit time. Our results support the findings of Miholic and colleagues (Miholic et al. 1989), who studied 11 patients with Roux-en-Y and 9 with jejunal interposition and found no association between "gastric" emptying time and postoperative weight gain. The lactulose breath test measures the transit of liquids and it has been shown that the transit of liquids and solids are independent (Malagelada et al. 1984). In most of our patients the transit time was easily identified in the time–expired hydrogen curves and the time when the rise in the breath hydrogen occurred was clearly distinguished from the earlier small-bowel bacterial overgrowth peak in the glucose breath test. However, it is possible that in some patients the caecum peak in the lactulose breath test represented bacterial overgrowth in the distal small intestine. Nonetheless the transit times in the respective study groups are comparable, since the bacterial overgrowth was equal in both groups assessed by the glucose breath test. The mean mouth-to-caecum transit time of 117 minutes in the pouch group and 110 minutes in the Roux-en-Y group is comparable with the median oro-caecal transit time of 110 minutes after total gastrectomy observed by Olbe and Lundell (1987) evaluated by the same method. Using a scintigraphic method Pellegrini and colleagues (1986) found a prolonged mouth-to-caecum transit time after total gastrectomy compared with control subjects (mean 298 minutes vs. 223 minutes).
There is no ideal means of measuring intestinal transit time available and there are many possible sources of error for different methods. Also in this study a wide deviation in the transit times of different patients was observed.

**Bacterial overgrowth**

A rise of at least 12 ppm within 2 hours and a high fasting breath $\text{H}_2$ level in the 50-g glucose breath test has been shown to be specific for bacterial overgrowth in the upper intestine (Kerlin and Wong 1988). Overgrowth was detected in every patient by culture after total gastrectomy in a small group of patients studied by Armbrecht’s group (1988). The hydrogen breath test has demonstrated elevated $\text{H}_2$ values after total gastrectomy comparable to those obtained in patients with achlorhydric atrophic gastritis and intragastric bacteria (Olbe and Lundell 1987).

The present results show that most patients (88%) after total gastrectomy do have bacterial overgrowth in the upper intestine as evaluated by the glucose breath test. Overgrowth was not more frequent among the patients with the pouch reconstruction than among those with Roux-en-Y reconstruction. The lack of gastric acid and altered intestinal motility in the Roux-en-Y reconstruction with or without pouch seems to result in bacterial overgrowth, which may be one of the main reasons for the malnutrition seen after total gastrectomy.

We detected a negative correlation between the maximal breath hydrogen concentration in the glucose breath test and the main nutritional parameters (serum albumin, blood haemoglobin, serum iron and postoperative weight loss). This may show the importance of bacterial overgrowth for the postoperative nutrition of patients after total gastrectomy. $\text{H}_2$ excretion between 60 and 180 minutes after standard meal (area under the curve) was correlated to the total concentration of bacteria in the gastric juice in a patient
group of achlorhydrics studied by Armbrecht and associates (1985). We used the maximal breath hydrogen concentration by reason of its simplicity to describe the amount of bacteria in the small intestine.

Bacterial overgrowth can lead to impaired micelle formation and bile salt deconjugation. Fat malabsorption after total gastrectomy was detected in 9 out of 11 patients by Walther and colleagues (1989a) studied by triolein breath test. Several other mechanisms for fat malabsorption have been proposed: loss of gastric emulsification of triglyceride, rapid passage of food and impaired pancreatic stimulation. The results here show that bacterial overgrowth is common after total gastrectomy and it may be more important than the change in the intestinal transit time. Shortened small-bowel transit seems to lead to severe dumping symptoms, but the transit time is not associated with malnutrition. Those patients who evinced higher or elevated alkaline phophatase activity demonstrated higher maximal concentrations in the glucose breath test. Since we did not measure the ALP isoenzymes in all patients it is impossible to say whether the elevated ALP activity comes from the bone or from the liver.

Pouchitis after colectomy and ileoanal pouch reconstruction in ulcerative colitis is a common condition and it is treated successfully by antibiotics. It has also been shown that ileoanal pouch patients have bacterial overgrowth in the pouch (Santavirta et al. 1991). There are only few studies of antimicrobial therapy of the bacterial overgrowth in the upper intestine (Suhr et al. 1990) and especially after gastric surgery. Armbrecht and associates (1985) could not show a decrease in symptoms after two weeks antimicrobial treatment in Billroth II patients, although H₂ levels in the breath test were significantly lowered. Probiotic treatment with lactobacillus fermentum was not effective compared with placebo in the treatment of intestinal bacterial overgrowth, but the patients evaluated were very heterogeneous, including only six after gastric surgery (Stotzer et al. 1996). Only two of our patients have been treated with
antimicrobial therapy for intestinal bacterial overgrowth after pathologic glucose breath test and symptoms. After the treatment the symptoms were alleviated and repeat breath test yielded normal findings in these two patients. At the moment duration, dosing and effect of antimicrobial therapy for bacterial overgrowth after total gastrectomy are open questions.

**Endoscopic and histological findings**

Pouchitis - bloody, loose stools with histologic changes of in the small bowel - is a major problem associated with ileoanal pouch reconstruction after proctocolectomy for ulcerative colitis (Becker 1993). In this present study no patient showed any endoscopic or histologic pouchitis-like changes. There were two patients, one in each group, with villous atrophy which could be reversed by gluten-free diet. This was not considered a form of pouchitis but previously unrecognised coeliac disease.
CONCLUSIONS

1. Jejunal pouch reconstruction may be safely performed without increased operative mortality. However, the procedure is more demanding than simple Roux-en-Y reconstruction, and special attention should be paid to the accomplishment of the oesophageal anastomosis.

2. Jejunal pouch reconstruction diminishes postoperative symptoms after total gastrectomy, especially during the first two postoperative years. Early satiety and dumping symptoms are less frequent in patients with a pouch. The symptoms diminish during the postoperative time and it seems that the adaptation process takes two to three years after total gastrectomy.

3. The emptying of solids is reduced to an abnormal level after jejunal pouch reconstruction. However, this does not result in obstructive symptoms such as vomiting, regurgitation, oesophagitis or notable bezoar formation. There is no difference in the emptying of liquids after pouch reconstruction compared with simple Roux-en-Y reconstruction.

4. Bacterial overgrowth is common after total gastrectomy. No difference prevails in this respect between pouch reconstruction and simple Roux-en-Y reconstruction. Bacterial overgrowth may be one of the main reasons for the malnutrition after total gastrectomy. Antibiotic and/or probiotic therapy should be evaluated in further studies.

5. Eating capacity is increased after pouch reconstruction compared with simple Roux-en-Y. This is reflected in larger and fewer meals consumed per day. This better eating capacity together with diminished postoperative symptoms might result in better quality of life, a matter of great interest in the future when the optimal reconstruction technique after total gastrectomy is sought.
6. Pouch reconstruction has no effect on the postoperative BMI or other nutritional parameters during a two-year follow-up, but later postoperatively the pouch seems to help to achieve and to maintain normal body weight. Pouch reconstruction may be associated with better calcium and vitamin D balance after total gastrectomy.

7. Pouch reconstruction is not associated with pouchitis-like complications and the pouch mucosa remains histologically normal in all patients. This mode of reconstruction is not associated with any long-term complications such as dilatation or obstruction, which could lead to reoperations or repeat surgery. However, our histological studies were only light- microscopic and in the future, assessment of possible ultrastructural changes in the pouch and comparison of these with ileoanal pouches would constitute an interesting line of inquiry.
SUMMARY
Since the first successful total gastrectomy in 1897, surgeons have sought the best mode of reconstruction for the patient. Roux-en-Y oesophagojejunostomy solved the problem of alkaline reflux oesophagitis, which was an inevitable complication after loop oesophagojejunostomy. In the Roux-en-Y method the duodenum is bypassed, which may partly compromise digestion and absorption, and some surgeons prefer interposition between the oesophagus and the duodenum instead of the Roux-en-Y method. Neither reconstruction offers any solution to the loss of the reservoir function of the resected stomach. Almost all gastrectomised patients suffer somewhat from fullness, upper abdominal pain and early satiety after meals. Furthermore, many suffer from malnutrition, anaemia and bone-metabolic disturbances.

The aims of the present study were to evaluate the operative mortality and morbidity associated with pouch reconstruction, to investigate the possible advantages of the pouch reconstruction, to assess the physiology of the upper intestine after this procedure, and to evaluate the long-term consequences of jejunal pouch reconstruction after total gastrectomy.

In a prospective, controlled study forty-nine gastric carcinoma patients were randomised for jejunal pouch reconstruction or simple Roux-en-Y reconstruction after total gastrectomy and data on mortality, morbidity, and postgastrectomy symptoms were collected systematically during the first two postoperative years. Operative 30-day mortality was zero in both groups, hospital stay was increased in the pouch group due to increased postoperative complications, predominately caused by the increased anastomotic leakage rate in the pouch group. After the randomised study the anastomotic operative technique was modified. During a two-year follow-up dumping and early satiety were diminished in the pouch group compared with Roux-en-Y. One patient was reoperated early in the series on account of relative obstruction in the distal part of the pouch. None of the patients suffered from endoscopic
oesophagitis. Dilatation for anastomotic stricture was used postoperatively in six patients, 3 after jejunal pouch reconstruction and 3 after simple Roux-en-Y. Bacterial overgrowth of the Roux-en-Y limb or the pouch was investigated by glucose breath test; 91% of the pouch patients and 86% of the Roux-en-Y appeared to have bacterial overgrowth in the upper intestine (NS). It may be assumed that this overgrowth is one important factor underlying malnutrition in the postgastrectomy patient and this should in future be evaluated.

A solid isotope emptying test was used to assess the motility of the pouch or Roux-en-Y limb. It emerged that emptying of both pouch and Roux-en-Y limb is decreased compared with normal the gastric emptying rate. The emptying rate in the pouch was significantly slower than that in the Roux-en-Y limb. However, patients appeared to have no symptoms related to this and only one bezoar was found five years after pouch reconstruction.

The small-intestinal transit time measured by the lactulose breath test was similar in both study groups (mean 110 minutes vs. mean 117 minutes) and thus pouch reconstruction would appear to reduces the passage of solids in the upper intestine but to have no effect on the passage of liquids in the gastrointestinal canal.

In order to evaluate the long-term consequences of a pouch reconstruction, 34 patients without recurrence were evaluated three years after total gastrectomy and 21 patients eight years postoperatively. Dumping and early satiety were diminished, and eating capacity improved in the pouch group at the three-year follow-up. In addition, weight loss was smaller and the patients ate fewer meals per day in this group. 25 (OH) vitamin D concentration tended to be higher and ALP activity lower in the pouch group. There were no long-term side-effects (oesophagitis, pouchitis, reoperations) from the pouch reconstruction during the eight-year follow-up.
In conclusion, the findings of this study show that jejunal pouch reconstruction offers cancer patients an acceptable reconstructional method after total gastrectomy. The advantages of the pouch reconstruction compared with simple Roux-en-Y are the following: diminishing of postoperative symptoms, improvement in eating capacity by one meal with fewer meals/day needed, decreased postoperative weight loss and possibly better postoperative nutrition. Although the emptying of solids from the pouch is reduced compared with the normal stomach and the Roux-en-Y reconstruction, the transit of liquids in the gastrointestinal canal is normal and the pouch does not seem to increase bacterial overgrowth of the upper intestine. Special attention should be paid to the surgical technique in performing the pouch-oesophageal anastomosis.
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APPENDIX

The questionnaires used during the two-year follow-up (Study I) at the outpatient clinic and in study IV

Study I

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<tr>
<td>GLUKOOSIHENGITYSTESTI</td>
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Study IV
Sukunimi..................................Etunimi........................................puh........................................

Osoite:...............................................................................................................................  

Viimeisen kahden viikon aikana minulla on ollut seuraavia oireita. Ympäröi oikea vaihtoehto.

1. Syömiseen liittyvä vatsakipua tai täyttymisen tunnetta
   ei ole ollut          on ollut lievänä       on ollut kohtalaisesti             on ollut paljon

2. Syömiseen liittyvä ( tai sen jälkeen tulevaa) heikotusta, hikoilua, sydämentykytystä, huonovointisuutta
   ei ole ollut          on ollut lievänä       on ollut kohtalaisesti             on ollut paljon

3. Ruoka on pyrkinyt tulemaan ylös esim. kumartaessa tai ruokasulaa on tullut suuhun tai on esiintynyt hankalaa röyhtäilyä
   ei ole ollut        on ollut lievänä       on ollut kohtalaisesti             on ollut paljon

4. Niellessä ruoka on tarttunut kiinni tai nieleminen on ollut vaikeata
   ei ole ollut          on ollut lievänä       on ollut kohtalaisesti             on ollut paljon

5. Minua on närästänyt tai on esiintynyt polttoa/ kirvelyä ylätapsalla tai rinnassa
   ei ole ollut          on ollut lievänä       on ollut kohtalaisesti             on ollut paljon

6. Suolentoimintani on ollut seuraavanlaista
   (ympäröi oikea vaihtoehto a-d)
   a. olen kärsinyt ummetuksesta
   b. suolen toiminnassa ei ole ollut ongelmia, suoli toimii 1-2 kertaa/vrk tai harvemmin
   c. suoli on toiminut mielestäni liian vilkkaasti tai ollut liian löysällä. Montako kertaa/vrk ? .................
   d. olen kärsinyt ripulista tai olen tarvinnut läääkitystä ripuliin

7. Tämän hetkinen painoni on .................kg   punnittu/ arvioitu
8. Pystyn yhden aterioinnin aikana (jos vertaan aikaan ennen mahalaukun poistoa = "normaali") syömään ilman vaivoja:
   a. alle puolet "normaalista" ateriasta
   b. puolet "normaalista" ateriasta
   c. kolme neljäosaa "normaalista" ateriasta
   d. keta kuinkin täyden aterian

9. Minulle on tehty "mahantähystys" viimeksi:
   kuukausi.............vuosi..............
   Missä tähystys tehtiin?.........................................................

10. Viimeisin hemoglobiiniarvoni on............. Milloin .................
     Muita laboratoriotuloksiani......................................................

11. Käytän rautalääkitystä: En / kyllä. Miten
     usein?.................................................................................


13. Käytän seuraavia vitamiineja, hivenaineita tai lisäravinteita:


15. Pääaterioideni lukumäärä on........./ vuorokausi
     Välipaloja syön keskimäärin............./ vuorokausi

     hoidettu? .................................................................
     Missä?........................................................................

17. Ruokahaluni on viimeisen 2 viikon aikana ollut yleensä (ympäröi oikea
     vaihtoehto)
   a. hyvä  b. kohtalainen, ei tyydyttävä  c. minulla ei ole ruokahalua

18. Muita oireita tai vaivoja, jotka mielestäni mahdollisesti liittyvät mahaan tai
     syömiseen? (jatka vapaasti kääntöpuolelle tai anna erillinen selvitys)
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