

A gastrectomy population: 25–30 years on

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Summary: Prior to 1960 a Polya gastrectomy was the most frequent operation for duodenal ulcer. The majority of these patients now have reached the age of sixty or older. A prospective longitudinal study of a cohort of patients who underwent gastrectomy between 1955 and 1960 was undertaken. Twenty five to thirty years later the study has revealed the extent of the nutritional problems that may arise with the passage of time and shows that these numerically far outweigh the mechanical post-gastrectomy syndromes and weight loss which tended to dominate the earlier post-gastrectomy scene.

By the end of the first decade, iron deficiency was the commonest nutritional problem. Vitamin B₁₂ deficiency assumed more importance in the second decade. During the third decade both reached equal prevalence, being found in some 90% of the female and 70% of the male residual population. Vitamin D deficiency and early osteomalacia was a lesser problem, reaching its climax in the second decade. Evidence suggested a high incidence of osteoporosis and this requires further investigation. Overall, women fared worse than men with a higher and earlier incidence of iron deficiency, particularly in the pre-menopausal group.

This study emphasizes the increasing need for regular screening of post-gastrectomy patients to detect early iron, vitamin B₁₂ and vitamin D deficiencies as patients grow older.

Introduction

Today in many centres a partial gastrectomy, whilst often the procedure of choice for gastric ulceration, is performed only occasionally for duodenal ulceration, a proximal gastric vagotomy or other vagotomy procedures having taken its place. Prior to 1960 however, a Polya gastrectomy was the most frequent operation for duodenal ulceration and many thousand operations were performed annually. The majority of these patients were early middle aged and now, 25–30 years on, have reached the age of 60 or older and form a considerable number of the elderly population. A prospective longitudinal study of a cohort of patients who underwent gastrectomy between 1955 and 1960 was undertaken to study the progress of such patients as they grew older. The primary purpose of the study was to determine the effect of the operation on overall nutrition, and in particular, the frequency and time of onset of deficiencies of iron, vitamin B₁₂ and vitamin D (early osteomalacia).

Patients

In 1969, 227 patients who had undergone partial gastrectomy for duodenal ulceration between 1955 and 1960 at University College Hospital in London were located. Of these 186 had undergone a Polya gastrectomy (141 males and 45 females) and 41 a Billroth I gastrectomy (24 males and 17 females). All agreed to attend a special follow-up clinic and since then only 17 have defaulted. The remainder continued to attend annually or more frequently for as long as they were able. Over the years, 37 have moved away, 41 have become unable to attend by virtue of age or frailty and 77 have died, leaving 52 still attending (40 men and 12 women). The average follow-up period was 20 years.

Methods

At each attendance the patients were seen by the same clinician (FIT) according to a standard proforma. They were weighed, a clinical history was taken with a dietary survey and any relevant physical examination related to symptoms was done. A record was made of capacity for food, the presence of diarrhoea and of post-gastrectomy mechanical syndromes. In addition X-ray examination of the right second metacarpal and faecal

This report is dedicated to Professor C.G. Clark who initiated and directed this study from 1968, and who sadly died on August 8th 1988.

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fat determinations were done on certain patients as mentioned later. Blood was taken for the following investigations: (1) full blood count; (2) serum iron and total iron binding capacity (TIBC) unless under treatment for iron deficiency; (3) serum B₁₂ unless under treatment for vitamin B₁₂ deficiency; (4) serum calcium, phosphate and alkaline phosphatase; (5) serum proteins (total, albumin and globulin).

These were aimed at the early detection of deficiencies of iron, vitamin B₁₂, prior to any anaemia and of vitamin D before the development of clinical osteomalacia.

Weight loss

Patients who were of ideal weight for age and height according to standard life tables before operation,¹ and those who were below ideal weight pre-operatively but regained their ideal weight after operation were regarded as normal. Patients who had lost weight pre-operatively and remained so post-operatively and those of normal weight pre-operatively who lost weight post-operatively were regarded as showing weight loss, the weight loss persisting throughout the follow-up despite dietary advice. Sustained post-operative fall of up to 4.5 kg was regarded as a moderate weight loss and above this as a severe weight loss.

Capacity for food

Persistent changes in the capacity for food were recorded. A moderately reduced capacity was regarded as being able to take half to one-third of what the patient would normally expect to eat at a meal, and severe as one-third or less.

Post-gastrectomy mechanical syndromes

These were classified as: (1) small stomach syndrome: patients who had reduced capacity for food associated with epigastric discomfort and vomiting accompanying any excessive intake of food. (2) Early dumping: symptoms of faintness, sweating and tiredness with hypotension 15–20 minutes after food. (3) Late dumping: symptoms as above, 30–40 minutes after food. (4) Bilious vomiting: bilious regurgitation or vomiting of bile after food.

Diarrhoea

Diarrhoea was classified as intermittent or continuous, and as moderate (up to 3 loose stools a day) or severe (more than 3 loose stools a day).

Steatorrhoea

At the first attendance all patients with diarrhoea and additional patients who were willing were investigated for faecal fat output using cuprous thiocyanate as a continuous marker² making a total of 158.

Mild steatorrhoea was regarded as an output of 6–12 g fat per day, and severe steatorrhoea as over 12 g.

Iron deficiency

Iron deficiency was defined as an iron saturation of less than 16%. A rise in TIBC often preceded a fall in serum iron by 3–4 months, and again the development of hypochromic anaemia occurred only after the iron saturation had fallen below 16% several months previously. This sequence enabled the detection of iron deficiency well before the appearance of any anaemia.^{3,4}

Vitamin B₁₂ deficiency

Vitamin B₁₂ deficiency was diagnosed when two separate bioassay estimations showed a value of less than 150 pg/ml.⁴ In most patients the fall in serum B₁₂ preceded any macrocytosis, neutrophil shift or anaemia.

Vitamin D deficiency

Vitamin D deficiency and early subclinical osteomalacia were more difficult to determine.^{5–7} Patients with a rising serum alkaline phosphatase, in whom liver disease, Paget's disease, bone secondaries or recent osteoporotic fractures had been excluded, were considered as possible cases of early osteomalacia. Initially bone biopsies were done on such patients but the availability of the expertise required to detect very early osteomalacia by the measurement of osteoid seams and calcification fronts was very limited. After 1974 additional information was obtained from a 24 hour urinary calcium output (below 2 mmol/24 h) when practicable on an outpatient basis and by serum alkaline phosphatase iso-enzyme electrophoresis showing that the enzyme was bony in origin. Plasma vitamin D levels were often equivocal. In suspected cases a therapeutic trial was given of calcium and vitamin D (BPC) tablets, 8/day for a period of 3 months. If the serum alkaline phosphatase fell to normal it was regarded as indicative of osteomalacia and a maintenance dose of 6 calcium and vitamin D tablets was continued.

Osteoporosis

Initially most of the patients were screened for any degree of osteoporosis in excess of normal changes for their age. This was attempted by calculating the Exton-Smith index of bone density from measurement of a standard X-ray of the second right metacarpal and identifying those below the ten percentile line for age and sex.⁸ In 1969, 216 patients were X-rayed. This was repeated on 147 in 1974 and on 82 patients in 1982.

Statistical methods

The results were expressed as percentage incidences and statistically analysed by the Chi square test with a Yates correction where appropriate or by the Fisher Exact test.

Results

Weight loss, capacity for food and post-gastrectomy syndromes

Following a 1–2 year settling-in period after the operation there was little change in the patients' age-adjusted weight status (Table I) or in their capacity for food. There were only a few patients whose diet was grossly deficient and in whom dietary advice resulted in a weight increase. Weight loss bore a close relationship to capacity for food and post-gastrectomy mechanical syndromes.

A moderately reduced capacity was found in 26% of males and 37% of females and a severely reduced capacity in 13% and 32% respectively. Post-gastrectomy syndromes did not feature any more in the group with moderately reduced capacity than in the whole series, but 88% of those with severely reduced capacity had mechanical syndromes.

Table I Overall incidence of persistent weight loss in patients after Billroth I or Polya gastrectomy with a M/F distribution stratified by degree of weight loss

Weight loss parameters†	Billroth I 24M/17F	Polya 141M/45F
Overall incidence of weight loss	39.0%	35.5%
Moderate	34.1%	28.0%
Severe	4.9%	7.5%
Male Moderate	37.5%	22.0%
Severe	4.2%	6.4%
Female Moderate	29.4%	46.7%*
Severe	5.9%	11.1%

†Moderate weight loss <4.5 kg; severe weight loss >4.5 kg; * $P < 0.005$ for male vs female for moderate weight loss in Polya group

Table II shows the incidence of post-gastrectomy syndromes. These became manifest soon after operation and tended to persist. They became a much smaller problem numerically later than iron or vitamin B₁₂ deficiency.

Steatorrhoea and diarrhoea

Mild steatorrhoea (6–12 g fat per day) was present in 14% and severe steatorrhoea (>12 g fat per day) in 20% of those investigated. There was no difference in the overall incidence of steatorrhoea between the Polya (37%) and the Billroth I (24%) groups of patients except that none of the Billroth I patients had severe steatorrhoea.

The pattern of diarrhoea when present remained consistent throughout the follow-up. None of the Billroth I patients complained of continuous diarrhoea but this was present in 5% of the Polya group, being a major problem in one male patient (0.5%). Moderate steatorrhoea was found in 20%

Table II Percentage incidence of post-gastrectomy syndromes

Post-gastrectomy syndrome	M/F	Overall 165M/62F	Polya 141M/45F	Billroth I 24M/17F	Polya vs Billroth I
Small stomach	Male	15.2%	7.0%	4.2%	NS
	Female	35.5%*	33.3%††	41.2%*	NS
Early dumping	Male	12.7%	3.5%	8.3%	NS
	Female	30.6%*	33.3%**	23.5%	NS
Late dumping	Male	1.8%	1.4%	4.2%	NS
	Female	4.8%	6.7%	0%	NS
Bilious vomiting	Male	8.5%	8.5%	8.3%	NS
	Female	17.7%	24.4%†	0%	$P < 0.02$

* $P < 0.001$, ** $P < 0.01$, † $P < 0.02$, †† $P < 0.05$ for males vs females overall and in the two gastrectomy groups.

and severe steatorrhoea in 50% of patients with continuous diarrhoea.

Sixty six per cent of patients with severe steatorrhoea lost weight, the loss being severe in 20%.

Iron, B₁₂ and vitamin D deficiencies

Interim reports have been made previously.^{3-6,9} The updated prevalence, allowing for patient loss at different times, for the male and female groups is shown in Table III and illustrated in Figure 1. There was no difference between Polya and Billroth I gastrectomies in either sex. It will be seen that iron deficiency occurred much earlier than B₁₂ deficiency, appearing in many patients during the first 10 years after operation. B₁₂ deficiency developed mostly 10 to 20 years after operation and slowly increased to equal iron deficiency by the end of 25 to 30 years,^{3,4,9} when approximately 70% of men and 90% of women had developed either iron or B₁₂ deficiency, the deficiencies being combined in 51% and 79% respectively. Vitamin B₁₂ deficiency had no relationship to deficient vitamin B₁₂ intake.

In men, the incidence of iron deficiency was higher in patients showing weight loss ($P < 0.02$), or reduced capacity for food ($P < 0.05$), but these differences were not seen in the women. The incidence of vitamin B₁₂ deficiency, although higher in those patients showing weight loss ($P < 0.01$), was unrelated to capacity for food or mechanical syndromes in either sex except that it was marked in patients with symptoms of bile reflux (33% vs 10% at 20 years, $P < 0.01$).

Iron deficiency was treated with ferrous gluconate 300 mg thrice daily for 2-3 months to restore the iron stores and then a maintenance dose of 300 mg daily was given to prevent recurrence.

Experience showed that ferrous gluconate was the best tolerated and best absorbed iron preparation in gastrectomy patients. Vitamin B₁₂ deficiency was treated by intramuscular injections of 1000 µg of hydroxocobalamin in alternative months.

A much smaller number of patients developed vitamin D deficiency, and this had become apparent in many patients during the first 10 years after operation.⁵⁻⁷ It occurred in 14/185 (7.5%) of Polya and 3/41 (7.3%) of Billroth I gastrectomies and was predominantly a problem of female patients (F:M = 19%:4%). Aversions to fat, including butter, milk or eggs were common after gastrectomy, especially in women patients and it is probable that these aversions combined with steatorrhoea contributed to the vitamin D deficiency. Fourteen of the 17 patients with early osteomalacia had faecal fat estimations. Mild steatorrhoea was found in 4 (28%) and severe steatorrhoea in 7 (50%), the respective figures for the whole series being 14% and 20% (*vide supra*).

Osteoporosis

The results have been published earlier,⁹ osteoporotic changes being present in the second right metacarpal in excess of normal ageing in those examined in 24%, 20%, 22% of men and 35%, 51%, 86% of women in 1969, 1974 and 1982 respectively.

Sex differences

From most aspects women patients seemed to do less well than men patients. There was a much higher incidence of severely reduced capacity for food, post-gastrectomy mechanical syndromes and

Table III Prevalence of iron or B₁₂ deficiency or osteomalacia in male and female patients

	1969	1978	1982	1984	1988
<i>Gastrectomy population</i>					
Total	227	141	91	79	52
Male	165	99	64	59	40
Female	62	42	27	20	12
<i>Iron deficiency</i>					
Male	31.5%*	61.6%	48.4%	62.7%	67.5%
Female	61.3%	59.5%	59.3%	80%	91.7%
<i>B₁₂ deficiency</i>					
Male	3.0%	19.2%	48.4%	59.3%††	70%
Female	0%	28.6%	59.3%	90%	83.3%
<i>Osteomalacia</i>					
Male	1.8%†	4.0%*	3.1%*	1.7%**	0%**
Female	11.3%	26.2%	29.6%	25%	33.3%

* $P < 0.001$, ** $P < 0.005$, † $P < 0.01$, †† $P < 0.025$ for males vs females.

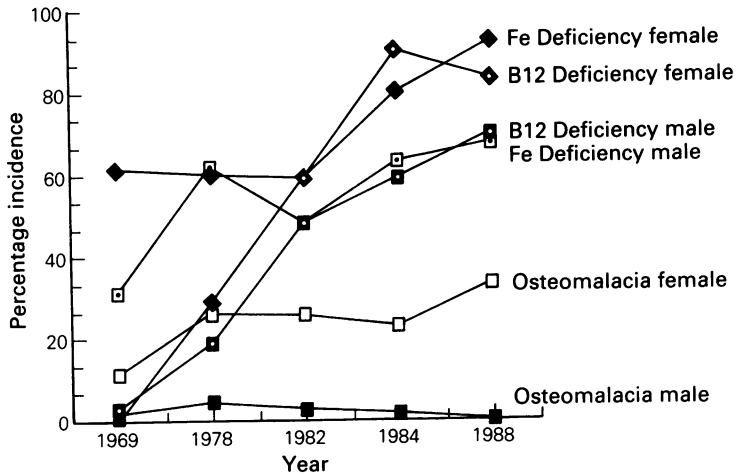


Figure 1 Prevalence of iron and B₁₂ deficiency and osteomalacia in male and female patients

aversions in the female patients. They fared worse also with regard to the incidence of iron and vitamin B₁₂ deficiency and even more markedly in the occurrence of vitamin D deficiency (Table III and Figure 1). The onset of iron deficiency appeared much earlier in the women patients, particularly in those who were pre-menopausal at the time of operation; it developed during the first 20 years in 81% (22/27) of the pre-menopausal compared with 63% (22/35) of the post-menopausal women.

Discussion

This study is unique in that it presents a continuous prospective follow-up of a gastrectomy population over 25–30 years and was aimed principally at the detection and treatment of iron, B₁₂ and vitamin D deficiencies before the development of anaemia or clinical osteomalacia. Previous studies have been reviewed by Fischer,^{10,11} who himself did a retrospective study of 1,025 Polya patients in 1977 22–30 years after operation, of whom he traced 423 patients.

The reported incidence of iron deficiency with anaemia varied from 5% to 62% in 11 studies reviewed by Fischer and from this present study it is apparent that this figure must vary according to the duration of follow-up. No other reports have shown a rising prevalence at different periods after gastrectomy of iron deficiency prior to the development of anaemia, this prevalence rising to 91.7% in females and 67.5% in males after 25 years. In comparison Small¹² (quoting Allan) reported that the prevalence of iron deficiency anaemia remained steady at 15–18% over a 20 year period.

Iron deficiency has been reported as occurring

more frequently when the duodenum has been bypassed¹³ but no difference was seen in this series between Billroth I and Polya gastrectomies.

Iron deficiency anaemia following a gastrectomy may be the result of several factors. One factor is the reduction of acid and pepsin secretion thus reducing the conversion of ferric to the more easily absorbed ferrous iron and of organic to inorganic iron. This is enhanced by uncontrolled rapid emptying which also allows the rapid passage over the principal sites of absorption in the duodenum and upper jejunum. Rapid emptying results in post-gastrectomy mechanical syndromes and reduced capacity for food and therefore one would expect a higher incidence of iron deficiency in such patients. This was demonstrated in the male patients but surprisingly not in the female patients in whom the onset was earlier, bearing a relationship to age at the time of operation and being more, though insignificantly so, in the pre-menopausal (81%) than in post-menopausal patients (63%).

Vitamin B₁₂ deficiency was reported as occurring in 10–50% of patients after gastrectomy in 7 studies reviewed by Fischer although he found none in his own series. Buxton¹⁴ reviewing 43 patients found an incidence of 56% at 10 years and 81% at 15 years, reporting that the earliest onset was 5½ years after operation. Deller and Witts¹⁵ reported a sharp fall in B₁₂ levels for the first 6 years which then levelled off. This series shows a rising prevalence with length of time after operation rising to 83.3% in women and 70% in men after 25 years.

Vitamin B₁₂ deficiency is related to stomach loss and not to uncontrolled emptying. It is enhanced by gastritis due to bile reflux. Another possible factor is competition for vitamin B₁₂ from bacterial

colonization of the afferent loop. The first two causes are demonstrated in this series by the absence of any relationship between capacity for food which is an index of uncontrolled emptying and by the significantly higher incidence in patients with symptoms of bile reflux. The incidence, however, was similar following Billroth I and Polya gastrectomies suggesting that the presence of a blind afferent loop is of lesser importance.

Most previous reports of post-gastrectomy osteomalacia have been concerned with clinical osteomalacia. Morgan and colleagues^{16,17} reported on the value of serum alkaline phosphatase estimations in the detection of osteomalacia. The detection of early or subclinical osteomalacia is obviously of great value in preventing the later onset of distressing pain and stress fractures, and this study shows the benefit of screening for an unexplained rise in serum alkaline phosphatase of bony origin and the value of a therapeutic trial of vitamin D and calcium to confirm a diagnosis.

It has long been suspected that osteoporosis in advance of normal ageing could be a major problem after gastrectomy.¹⁸ Morgan and colleagues^{16,17} found a reduced cortical width in the mid point of the second right metacarpal in 11% of patients between the ages of 40–59 more than 10 years after gastrectomy and in 28.5% of those aged over 60, the onset being earlier in women. More recently Paakkonen and colleagues¹⁹ described a significant reduction in bone density using the Am gamma ray attenuation method in all of 18 Billroth I and 19 Polya gastrectomy patients examined 24–29 years after operation. The Exton-Smith formula⁸ for detecting osteoporosis based on measurements of the second right metacarpal has been superseded by more sophisticated methods such as photon absorptiometry and quantitative computerized tomography which were not available to us at the time of this study. It needs to be remembered that osteoporosis is another important effect of gastrectomy and its magnitude needs to be determined and further studies are now in progress. Unfortunately no adequate preventive or therapeutic treatment is yet available.

The association between steatorrhoea and weight loss has been well documented and reviewed by Hillman.²⁰ Steatorrhoea is a major factor in vitamin D deficiency and reduced calcium absorp-

tion. Paakkonen and colleagues¹⁹ report of a 25% incidence after 10 years. In this series the occurrence of severe steatorrhoea (> 12 g/day) only in Polya and not in Billroth I patients suggests that the loss of duodenal continuity is important. The presence of an afferent loop results in both pancreatico-cibal asynchrony with a delay in pancreatic enzymes reaching the food during its passage down the small intestine²¹ and also the inactivation of the lipase from bacterial contamination in the loop.²²

The incidence of weight loss and of post-gastrectomy syndromes presented early on during this study corresponded with that of other series.^{11,12,23–25} In the course of time they became a much smaller problem numerically than iron and vitamin B₁₂ deficiencies.

In conclusion, this study demonstrates the increasing prevalence particularly of iron and of vitamin B₁₂ deficiency in a gastrectomy population, reaching approximately 75% in 20–30 years. This stresses the importance of regular screening for both iron saturation and vitamin B₁₂ levels to anticipate the development of severe deficiency, the importance of this rising with passing years. In addition, at the end of the first decade any unexplained joint or bone pains, or pathological fractures may be a result of osteomalacia, and this again can be anticipated by regular screening of serum alkaline phosphatase with further investigation of those patients with rising levels.^{5,6}

It is important now that gastrectomy is performed less frequently, not to forget the large number of gastrectomy patients still alive in whom late nutritional deficiencies may develop. These patients should be annually screened and the need for this increases in importance with advancing age.

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