

# Treatment and prevention of lymphorrhea after radical gastrectomy of gastric cancer

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## Abstract

**Purpose** Lymphorrhea is an uncommon complication of abdominal surgery. Here, we retrospectively investigate the treatment and prevention of lymphorrhea after radical gastrectomy.

**Methods** From January 1995 to January 2007, a total of 1,596 patients who underwent surgery for gastric cancer were investigated. According to the AJCC cancer stage manual, tumor stages of 693 (43.4%) cases were T1 or T2 and 903 (56.6%) cases were T3 or T4. A total of 1,104 (69.2%) patients received grade D1 lymphadenectomy or grade D2, and 492 (30.8%) patients received grade D3 or D4. Ligation was used during the lymphadenectomy in 829 (51.9%) patients, and the electrocautery was used in 767 (48.1%) patients. Patients diagnosed of lymphorrhea were treated with total parenteral nutrition (TPN) alone before 2001, and with TPN plus octreotide after 2001.

**Results** The incidence of lymphorrhea of patients with D1–2 lymphadenectomy was much lower than those with D3–4 lymphadenectomy ( $P < 0.01$ ). For patients whose lymphatic vessels were ligated during the operation, the incidence of lymphorrhea was much lower than those lymphatic vessels were electrically cauterized ( $P < 0.01$ ). No significant difference of incidence of lymphorrhea could be found between patients with T1–2 and T3–4 tumor stages ( $P > 0.05$ ). Octreotide or TPN administration can reduce the quantity and duration of lymphorrhea, and the combina-

tion of Octreotide and TPN has a more significant effect on lymphorrhea than TPN alone ( $P < 0.01$ ).

**Conclusion** The major cause of lymphorrhea following radical gastrectomy was the inappropriate management of lymphadenectomy. Avoiding an extensive lymphadenectomy at surgery and ligating the disrupted lymph vessels would reduce the incidence of lymphorrhea. The combination of Octreotide and TPN is an effective therapeutic modality for lymphorrhea.

**Keywords** Stomach neoplasma · Lymph node excision · Lymphorrhea · Octreotide · Total parenteral nutrition

## Introduction

Postoperative lymphorrhea has been observed after retroperitoneal lymphadenectomy for urinary oncological surgery (Ferrigini and Novicki 1985), portal system decompression (Maywood et al. 1978), abdominal aortic surgery (Williamson and Provan 1987), renal transplantation (Liu et al. 2006), and after arthrodesis using an anterior approach to the spine (Shen et al. 1989). The incidence of lymphorrhea was approximately 7.4% after oncological abdominal surgery (Kaas et al. 2001), however, only a few cases of lymphorrhea after radical gastrectomy for gastric cancer have been reported. (Iankin. 2006; Tanaka et al. 2004) Lymph node metastases occur during the early stages of gastric cancer, and regional lymphadenectomy is recommended as a part of radical gastrectomy.

Recently, beneficial effects have been reported by the use of octreotide in the treatment of lymphorrhea after axillary node dissection (Carcoforo et al. 2003). Here, we try to investigate the treatment and prevention of lymphorrhea after radical gastrectomy retrospectively.

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## Materials and methods

We retrospectively reviewed 1,596 patients who underwent surgery for gastric cancer from January 1995 to January 2007. All the patients underwent routine biochemical and physical examinations before operation. Those who died within 2 weeks of the operation and those with anastomotic leakage, abdominal infection, and ileus were excluded from this study. According to the AJCC cancer stage manual (6th edn, 2003), tumor stages of 693 (43.4%) cases were T1 or T2 and 903 (56.6%) cases were T3 or T4. A total of 1,104 (69.2%) patients received grade D1 lymphadenectomy (perigastric lymph node dissection) or grade D2 (standard lymph node dissection), and 492 (30.8%) patients received grade D3 (extended lymph node dissection) or D4 (far-extended lymph node dissection including the paraaortic lymph nodes). Ligation was used during the lymphadenectomy in 829 (51.9%) patients, and the electrocote cautery was used in 767 (48.1%) patients.

Diagnostic criteria of lymphorrhea included: (1) abdominal drainage was more than 200 ml per day and over 3 days after radical gastrectomy; (2) drainage was non-blood and amylase in normal level; (3) the drainage was confirmed as lymph fluid by chylous qualitative and triglyceride tests.

Patients diagnosed of lymphorrhea were treated with total parenteral nutrition (TPN) alone before 2001, and with TPN plus octreotide (longastatina, ITALFARM, Srl, Italy; 0.1 mg three times a day subcutaneously) after 2001. We reviewed the incidence of lymphorrhea in different surgical procedures, the daily amount of lymphorrhea in the first 7 days and the duration of drainage in the two groups.

All values were expressed as mean  $\pm$  SD, Chi-squared test and Student's *t* tests were used to determine the significance of the differences among the groups. Statistical calcu-

lations were performed with SPSS (version 12.0). A *P* value of less than 0.05 was considered statistically significant.

## Results

A total of 53 patients (53/1,596, 3.32%) presented with lymphorrhea after radical gastrectomy in our study. The incidence of lymphorrhea of patients with D1–2 lymphadenectomy (22/1,104, 1.99%) was much lower than those with D3–4 lymphadenectomy (31/492, 6.30%) ( $P < 0.01$ ). In addition, for patients whose lymphatic vessels were ligated during the operation, the incidence of lymphorrhea was much lower than those lymphatic vessels were electrically cauterized (14/815, 1.72% vs. 39/728, 5.36%, respectively) ( $P < 0.01$ ). However, no significant difference of incidence of lymphorrhea could be found between patients with T1–2 and T3–4 tumor stages (26/667, 3.90% vs. 27/876, 3.08%, respectively) ( $P > 0.05$ ) (Table 1). Moreover, we found the incidence of lymphorrhea of patients was also closely associated with grade of lymphadenectomy and did not associated with tumor stages either in ligation group ( $P < 0.05$ ,  $P > 0.05$ ) or in electrocote cautery group ( $P < 0.01$ ,  $P > 0.05$ ) (Table 2).

Patients in the TPN alone group had an average amount of  $455.68 \pm 45.94$  ml per day in the first 7 days after operation and an average duration of  $23.32 \pm 9.62$  days. In comparison, patients in the TPN plus octreotide group had an average amount of  $274.84 \pm 36.23$  ml per day and an average duration of  $7.32 \pm 2.87$  days ( $P < 0.01$ ,  $P < 0.01$ ). By day 7, the drains were removed from 66.67% of patients in the TPN plus octreotide group which showed significant difference with TPN alone group (3.12%,  $P < 0.01$ ) (Table 3).

**Table 1** Relationship of lymphorrhea with grade of lymphadenectomy, surgical procedures and tumor stages

| Lymphorrhea | Lymphadenectomy |      |                | Surgical procedures |     |                | Tumor stages |      |                |
|-------------|-----------------|------|----------------|---------------------|-----|----------------|--------------|------|----------------|
|             | D1–2            | D3–4 | <i>P</i> value | Lig                 | EC  | <i>P</i> value | T1–2         | T3–4 | <i>P</i> value |
| Yes         | 22              | 31   |                | 14                  | 39  |                | 26           | 27   |                |
| No          | 1082            | 461  | <0.01          | 815                 | 728 | <0.01          | 667          | 876  | >0.05          |

*Lig* ligation, *EC* electrocote cautery

**Table 2** Relationship of lymphorrhea with grade of lymphadenectomy and tumor stages in ligation group and electrocote cautery group

| Lymphorrhea | Lig ( <i>n</i> = 829) |      |                |      |      |                | EC ( <i>n</i> = 767) |      |                |      |      |                |
|-------------|-----------------------|------|----------------|------|------|----------------|----------------------|------|----------------|------|------|----------------|
|             | D1–2                  | D3–4 | <i>P</i> value | T1–2 | T3–4 | <i>P</i> value | D1–2                 | D3–4 | <i>P</i> value | T1–2 | T3–4 | <i>P</i> value |
| Yes         | 5                     | 9    |                | 5    | 9    |                | 17                   | 22   |                | 21   | 18   |                |
| No          | 540                   | 275  | <0.05          | 363  | 452  | >0.05          | 542                  | 186  | <0.01          | 304  | 424  | >0.05          |

*Lig* ligation, *EC* electrocote cautery

**Table 3** Clinical character of TPN alone group and TPN + Octreotide group

|                                                            | TPN ( <i>n</i> = 32) | TPN + Octreotide ( <i>n</i> = 21) | <i>P</i> value |
|------------------------------------------------------------|----------------------|-----------------------------------|----------------|
| Mean amount of lymphorrhea per day in the first 7 days(ml) |                      |                                   |                |
| Mean ± SD                                                  | 455.68 ± 45.94       | 274.84 ± 36.23                    | <0.01*†        |
| Range                                                      | 350.00–520.00        | 220.00–370.00                     |                |
| Duration of drainage                                       |                      |                                   |                |
| Mean ± SD                                                  | 23.32 ± 9.62         | 7.32 ± 2.87                       | <0.01*†        |
| Range                                                      | 7.00–38.00           | 5.00–19.00                        |                |
| Duration of drain placement                                |                      |                                   |                |
| ≤7 days                                                    | 1(3.12%)             | 14(66.67%)                        | <0.01*‡        |
| >7 days                                                    | 31(96.88%)           | 7(33.33%)                         |                |

SD standard deviation, HB hemoglobin, TPN total parenteral nutrition  
 \*Significant values, †Student’s *t* test, ‡Chi-squared test

The side effects of octreotide in our study were minimal which included local irritation at the infection site and general nonspecific gastrointestinal discomfort (anorexia, abdominal cramps, steatorrhea, and diarrhea). Hyperglycemia can pose an important concern lonely with more chronic treatment. None of these adverse effects led to discontinuation of the treatment.

**Discussion**

Causes of lymphorrhea after gastric cancer surgery

There are numerous causes of lymphorrhea, and the main cause is the surgical procedure used but not tumor stages. We ligated only the large visible disrupted lymph vessels during lymphadenectomy. The lymphatic leaks from the stumps of the small and invisible lymph vessels into the free abdominal cavity resulting in lymphorrhea. The more extensive the lymph node dissected, the higher incidence of lymphorrhea will be. It has been reported in literature that the incidence of lymphorrhea is approximately 1.2–3.0% after retroperitoneal mesenteric vessel pedicle lymph node dissection (Halkic et al. 2003). In this study, the incidence was 1.99% in the patients with D1–2 lymphadenectomy, however, the incidence was as high as 6.30% in the patients with D3–4 lymphadenectomy, indicating that extensive lymph node dissection leads to a higher incidence of lymphorrhea. From this data, we considered that the cause of the higher incidence of lymphorrhea in the patients with D3–4 lymphadenectomy as compared to that in patients with D1–2 lymphadenectomy was the more extensive lymph node dissection in the former, leading to a greater number of injured lymph vessels. The study also showed that the incidence of lymphorrhea was significantly higher

in the patients in whom the electrotonic cautery was used than in those ligation was used. The electrotonic cautery cannot completely seal the large disrupted lymph vessels and lymph vessels with large drainage volumes. The scars on the lymph vessel stumps after cauterization can disintegrate due to the increased lymph fluid pressure, this can lead to the leakage of lymph fluid from the stump. We failed to find any relationship between the incidence of lymphorrhea and tumor stages.

The prevention of lymphorrhea after gastric cancer surgery

During lymph node dissection for gastric cancer, the cisterna chyli or the surrounding lymph vessel network can be injured. Particularly, in D3–4 dissections, the lymph vessel network around the abdominal aorta, inferior caval vein, and mesenteric vessels can be easily injured. Therefore, during operation, we should carefully dissect and individually ligate the divided tissues. The study indicated that ligation by using a thread could reduce the incidence of lymphorrhea. The electrotonic cautery, which only effectively seals the smaller lymph vessels, may lead to lymphorrhea. However, ultrasonically activated shears might reduce the incidence of lymphorrhea (Tsimoyiannis et al. 2002).

It has been reported that as compared to the patients with D1–2 lymphadenectomy, the average daily amount of intra-abdominal fluid collected was higher and the duration of lymphorrhea was longer in patients with D3–4 lymphadenectomy. The postoperative quality of life was significantly decreased with lymphorrhea (Davies et al. 1998). Therefore, selecting a D1–2 lymphadenectomy for early or partially advanced gastric cancer could not only avoid early postoperative recurrence and increase the rate of radical cure but also reduce postoperative lymphorrhea which resulting in a better quality of life.

The treatment of lymphorrhea after gastric cancer surgery

TPN can dramatically decrease the lymph flow in the thoracic duct from 220 ml/(kg h<sup>-1</sup>) to 1 ml/(kg h<sup>-1</sup>) (Aalami et al. 2000). Moreover, TPN can restore the nutritional deficits and balance the metabolic impairments imposed by long-standing lymphorrhea. Therefore, TPN are essential in the operative management of lymphorrhea. The curative effect of an MCT oil low-fat diet was only 36%, and the treatment duration was relatively long, requiring 4–6 months for adequate effect (Bhatia et al. 2001). TPN can reduce the accumulation of intra-abdominal lymph fluid, decreasing the loss of albumin and other nutrients that are induced by abdominal paracentesis, and it can simultaneously supply the necessary nutrition and rectify the fluid and electrolyte balance and hypoproteinemia. A satisfactory effect can be obtained in 3–4 weeks of this treatment.

The mechanism by means of octreotide affects lymphorrhea is unknown. It has also been speculated that somatostatin improves chylous ascites by inhibiting lymph fluid excretion through specific receptors found in the normal lymphatic vessels of the intestinal wall (Shapiro et al. 1996; Reubi et al. 1992). However, somatostatin receptors have been found in lymphatic tissues also outside the gastrointestinal tract (Harris 1990; Ulíbarri et al. 1990; Reubi et al. 1993), so it is possible that there should be a direct action on lymphatic vessels. Somatostatin has previously been shown to decrease the intestinal absorption of fats, lower the triglyceride concentration in the thoracic duct, and attenuate lymph flow in the major lymphatic channels (Collard et al. 2000).

In present study, the mean amount of drainage per day in the first 7 days was significantly lower in the TPN plus octreotide group ( $P < 0.01$ ) which indicates the therapeutic effect of somatostatin. By day 7, the drains were removed from 66.67% of patients in the TPN plus octreotide group which showed significant difference with TPN alone group ( $P < 0.01$ ). This result may help in reducing the dose of octreotide and consequently the cost of treatment which might be tailored according to the amount and duration of drainage. The total period of drainage was much lower in the TPN plus octreotide group ( $P < 0.001$ ). The significant decrease in the amount and duration of drainage association with negligible side effects and less infection rate by use of octreotide may improve patient's quality of life, shorten hospital stay, and give the chance for early adjuvant treatment to be started.

In conclusion, this study indicates that combination of Octreotide and TPN was an effective therapeutic modality for postoperative lymphorrhea and should be a first-line therapy. This therapy should be initiated as early as possible after the diagnosis.

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