



## Outcomes of a Randomised Controlled Trial (Feasibility Study) of Prophylactic Pyloric Balloon Dilatation during Ivor Lewis Esophagectomy to Prevent Delayed Gastric Emptying

Mohamed Abdelrahman<sup>1\*</sup>, Helen Neilens<sup>2</sup>, Victoria Yates<sup>2</sup>, Amber Lorde<sup>2</sup>, Arun Ariyathenam<sup>1</sup>, Richard Berrisford<sup>1</sup>, Grant Sanders<sup>1</sup>, Lee Humphreys<sup>1</sup>, Grant Sanders<sup>1</sup>, Ji Tham<sup>1</sup>, Tim Wheatley<sup>1</sup> and David SY Chan<sup>1</sup>

<sup>1</sup>Department of Upper GI Surgery, Derriford Hospital, Plymouth, United Kingdom

<sup>2</sup>Department of Research and Development, Derriford Hospital, Plymouth, United Kingdom

\*Corresponding Author: Mohamed Abdelrahman, Department of Upper GI Surgery, Derriford Hospital, Plymouth, United Kingdom.

**Received:** March 19, 2024

**Published:** March 28, 2024

© All rights are reserved by **Mohamed Abdelrahman., et al.**

### Abstract

Early delayed gastric emptying (DGE) occurs in up to 37% of patients following esophagectomy. This can contribute to increased anastomotic leak and respiratory infection rates. Although the treatment of DGE in the form of pyloric balloon dilatation (PBD) post-operatively is well established, there is no consensus on the optimal approach in the prevention of DGE. The aim of this study was to determine the feasibility of a randomised controlled trial comparing prophylactic pyloric balloon dilatation (PBD) to no intervention (control group) on the rates of delayed gastric emptying (DGE). All 20 patients approached were successfully randomised (PBD: n=10, Control: n=10). All outcome measures were successfully measured. This study opens the door for a future full RCT study comparing the effect on outcomes of DGE, between prophylactic PBD and no intervention in patients undergoing esophagectomy.

**Keywords:** Feasibility Study; Prophylactic Pyloric; Balloon Dilatation; Ivor Lewis; Esophagectomy; Gastric Emptying

### Introduction

The Ivor Lewis gastro-esophagectomy is a complex operation that is performed to treat cancer of the esophagus [1]. As survival figures have improved [2], more focus on short term and long-term morbidity has emerged. Delayed gastric emptying (DGE) is one of these complications and has an incidence of up to 37% [3].

It has been established via a systematic review and meta-analysis that there is some evidence supporting decrease in post esophagectomy early DGE after prophylactic PBD [4-7]. Furthermore, our local definition, at University Hospital Plymouth (UHP), of early DGE is comparable to the IEC definition [8,9]. The safety of PBD was confirmed in previous studies [10]. We have published a protocol for the feasibility RCT study, comparing the effects on

DGE between prophylactic PBD and no intervention [11]. It has been established and was accepted by the HRA ethics committee. The aim of this study is to convey the results of this feasibility study and establish that carrying out an RCT as noted above is achievable.

### Methods

#### Patient selection

Patients who underwent esophagectomy for cancer at University Hospital Plymouth (UHP) between January 2022 to April 2022 were approached to be recruited to the study. Once recruited, they were randomised (sealed envelope programme) to either the control group (no pyloric dilatation) or prophylactic pyloric balloon dilatation (PBD group).

**Primary objectives**

As a feasibility study, the objectives will be to ascertain the following:

- Number of patients approached.
- Number of patients who agreed to be randomised.
- Number of patients successfully randomised.
- Number of patients who dropped out.
- Successful measurement of outcome measures

**Secondary objectives**

Assessment of process and procedure of study such as

- Blinding of the research team
- Completion of quality-of-life questionnaire by patients

**Outcome measures**

- Rate of delayed gastric emptying
- Rate of anastomotic leak
- Rate of pneumonia

Early delayed gastric emptying (DGE)	University Hospital Plymouth (UHP) [8]
Clinical definition	24-hour nasogastric output greater than 50% of total oral fluid intake in that period measured on morning of day four on wards post-surgery
Radiological definition	Conduit dilation greater than 50% of the right hemi-thorax at day four post-surgery (patients have daily x-rays apart from day 2 post-surgery)

**Table 1:** Definition of early delayed gastric emptying (UHP).

**Post-operative protocol**

An ERAS protocol was implemented [8]. Patients are encouraged to mobilise early with intensive physiotherapy.

**Diagnosis of delayed gastric emptying**

The UHP definition of delayed gastric emptying outlined in Tables 1 was used to diagnose patients with early DGE.

**Treatment of delayed gastric emptying**

Patients diagnosed with DGE were either managed conservatively or underwent endoscopy and pyloric balloon dilatation [10].

This was done no earlier than seven days after surgery to avoid harm to the anastomosis. Endoscopic pyloric dilatation was carried out under general anaesthetic. A 30 mm CRETM Fixed Wire Balloon Dilator (Boston Scientific), which had a total length of 90 cm was the mainstay of management. Once the pylorus is traversed, a guide wire is inserted via the working channel. Under X-ray guidance, the balloon is passed over the wire and dilated fully for 2 minutes. Chest X-rays were performed daily following dilatation to confirm reduction of conduit size to less than 50% of the right hemi-thorax. Naso-gastric tubes were removed or left behind according to individual surgeon preference. Morbidity was classified according to the Clavien-Dindo criteria [12].

**Follow-up**

Patients are reviewed after discharge at 2 weeks, then 3 months for the first year. Thereafter they are reviewed every 6 months to complete an overall 5-year follow-up. The assessment for the study looked at the index admission and if there were any delayed dilations later after discharge.

**Statistical analysis**

Grouped data were expressed as median (range) and comparison was carried out using non-parametric methods. X<sup>2</sup> test was used for comparison of categorical variables. Comparison of continuous variables was carried out with the Mann-Whitney U-test. A level of statistical significance was set at P value of <0.05.

**Results**

**Primary objectives**

Table 2 shows the characteristics of patients who underwent esophagectomy. As per the ethical committee recommendation the target of the study was to approach 20 patients. This was done and all 20 patients approached agreed to be randomised. Successful randomisation was carried out using the sealed envelope computer programme. Ten patients were successfully randomised to the control group and ten patients to the PBD group (Figure 1).

Three patients (15%) were excluded as the tumour was not traversed during endoscopy. All three belonged to the control group. No patients dropped out of the study and outcome measures were successfully acquired.

Characteristics	Overall	PBD	Control	p-value
Total number	20	10	10	
Median Age, years (range)	66.5 (35-75)	67.5 (35-75)	63(51-74)	0.35
Male: Female- no. (%)	17:3 (85:15)	9:1 (90:10)	8:1 (88.9:11.1)	0.94
Tumour Type- no. (%)ACA: SCC	17:2 (85:10)	10:0 (100:0)	7:2 (77.8 :22.2)	0.41
Operative approach no. (%)				
Hybrid: Open: inoperable	13:6:1 (65:30:5)	9:1 (90:10)	4:5 (44.4:55.6)	0.10
Pathological T stage no. (%)				0.81
pT0	3 (15)	2 (20)	1 (11.1)	
pT1	5 (25)	3 (30)	2 (22.2)	
pT2	1 (5)	1 (10)	0	
pT3	10 (50)	4 (40)	6 (66.7)	
pT4				
Pathological N stage no. (%)				0.78
N0	11 (55)	5 (50)	6 (66.7)	
N1	4 (20)	2 (20)	1 (11.1)	
N2	2 (10)	1 (10)	2 (22.2)	
N3	2 (10)	2 (20)	0	
ASA no. (%)				0.26
2	12 (60))	7 (70)	4 (44.4)	
3	8 (40)	3 (30)	5 (55.6)	
Median BMI, Kg/m2, (Range)	26 (19.8-42.6)	25.9 (15.2-38.6)	31 (19.8-25.5)	0.33

**Table 2:** Characteristics of patient cohort who underwent esophagectomy.

### Secondary objectives

Blinding of patients to which group they belonged to was successful. Not all research member of the team were successfully blinded as some were part of the clinical team performing the procedures. All patients completed the initial quality of life (QOL) questionnaire. Eight patients completed the 2- week QOL questionnaire. Twelve patients completed the 3-month QOL questionnaire.

### Outcome measures

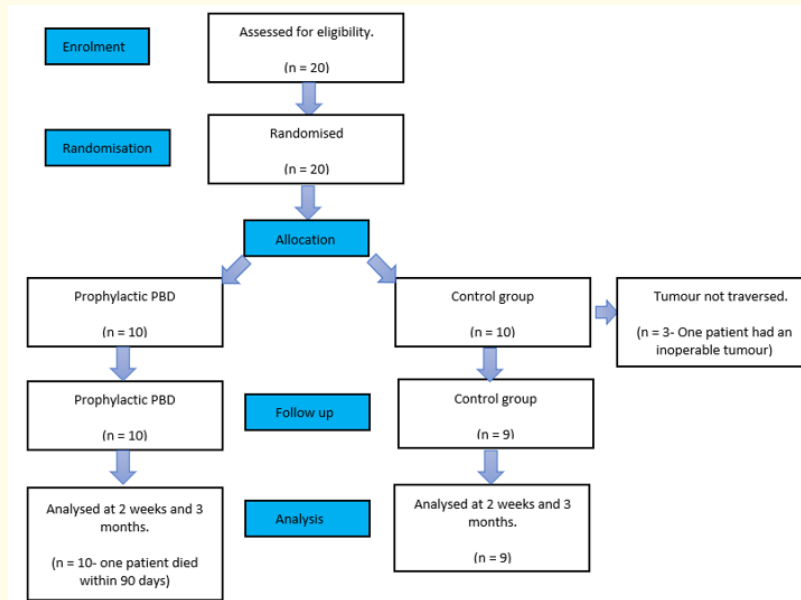
Table 3 shows outcomes for delayed gastric emptying, anastomotic leak and pneumonia in both groups. One patient died within 90 days post operatively.

### Discussion

This study has shown that carrying out a randomised control trial comparing prophylactic PBD to a control group is feasible. All

the patients approached have been randomised successfully. All primary objectives were achieved. The trial was able to collect the required data for both primary and secondary outcomes.

The difficulty in prevention and management has always been the definition of DGE post esophagectomy. There has been no consistent definition in all the studies that assessed prophylactic PBD. An international consensus introduced a joint Delphi process to introduce a definition of DGE [9]. In UHP a definition of DGE was originally introduced [8]. Both definitions were applied to assess PBD in patients in this study. The validation of the international definition remains in question when applied to the UHP population retrospectively.



**Figure 1:** Consort diagram of patients undergoing esophagectomy. PBD: Pyloric Balloon Dilatation

Outcomes	PBD	Control	p- value
Median endoscopy time, minutes (range)	9.19 (3-16)	1 (2.33-5)	0.46
Delayed gastric emptying (% - check)	1 (10)	2 (20)	0.53
Anastomotic leak	3	1	0.31
Conservatively.	2	1	
Relook thoracotomy	1	0	
Pneumonia	1	1	1
Length of stay	8 (7-28)	8 (7-61)	0.66

**Table 3:** Outcomes of patient cohort who underwent esophagectomy.

Prevention of DGE post esophagectomy has always been under question in the literature. From difficulty of an agreed definition to which procedure is the most successful [13]. Many believe that preventative methods are more important than curative measures [14]. Initially the use of whole stomach as a conduit has been shown to be associated with increased gastric capacity, better vasculature, fewer meals and snacks per day, faster eating and fewer complaints of early satiety [15-17]. More work however showed that a tubular conduit which is straight, and narrow was more advantageous. It avoided redundancy and therefore was associated lower incidence of postoperative reflux esophagitis and thoracic stomach syndrome [18]. This was more evidence in addition to historic literature that

showed a tubular stomach demonstrated a faster emptying rate [19]. The question however that has always played a big role in the literature is whether a pyloric drainage procedure was required. An experimental study comparing flow visualization models using different sized acrylic based photopolymer tube grafts with different pyloric openings led the authors to suggest that a narrow tube and/or pyloric drainage procedure would be better for gastric emptying [20]. Systematic reviews however concluded that pyloroplasty and botulinum injection had no significant effect on DGE [13,21].

Pyloric balloon dilatation has been the mainstay post-operative treatment for DGE [10]. The role of prophylactic pyloric balloon dilatation (PBD) however is not well established as a prevention of DGE. A previous study carried out by our group has shown that prophylactic PBD reduces the incidence of both DGE and anastomotic leak [7]. This however was a meta-analysis of observational studies [4,5,22]. There have been no randomised controlled trials to assess the effect of prophylactic PBD.

The strength of the study is the randomisation of patients and therefore level 1 evidence. The main limitation of the study is the low number of patients, however this was recommended by the ethics committee, as they felt this was sufficient to answer the question of feasibility regarding the primary objectives. It is evident that an RCT comparing prophylactic PBD to control is feasible which opens the door to carrying out a full RCT in the future.

## Conclusion

A successful feasibility trial has been carried out which opens the door for a full RCT study comparing the effect on outcomes of DGE, between prophylactic PBD and no intervention in patients undergoing esophagectomy.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The study is sponsored by University Hospital Plymouth (Derriford Hospital). The hospital Research and Development department has been involved in preparation of the protocol and on ethics application.

## Bibliography

1. LEWIS. "The surgical treatment of carcinoma of the oesophagus; with special reference to a new operation for growths of the middle third". *British Journal of Surgery* 34 (1946): 18-31.
2. M Konradsson and M Nilsson. "Delayed emptying of the gastric conduit after esophagectomy". *Journal of Thoracic Disease* 11 (2019): S835-S844.
3. Deldycke E Van Daele., et al. "Functional outcome after Ivor Lewis esophagectomy for cancer". *Journal of Surgical Oncology* 113 (2016): 24-28.
4. EW Swanson., et al. "Endoscopic pyloric balloon dilatation obviates the need for pyloroplasty at esophagectomy". *Surgical Endoscopy* 26 (2012): 2023-2028.
5. E Hadzijasufovic., et al. "Preoperative endoscopic pyloric balloon dilatation decreases the rate of delayed gastric emptying after Ivor-Lewis esophagectomy". *Diseases of the Esophagus* 32 (2019): 18.
6. C Decker., et al. "Gastric emptying after esophagectomy: comparing single therapy versus dual therapy method for pyloric drainage". *Shanghai Chest* 4 (2020): 37-37.
7. M Abdelrahman., et al. "Systematic review and meta-analysis of the influence of prophylactic pyloric balloon dilatation in the prevention of early delayed gastric emptying after oesophagectomy". *Diseases of the Esophagus* (2021).
8. JC Tham., et al. "Intraoperative pyloric botulinum toxin injection during Ivor-Lewis gastroesophagectomy to prevent delayed gastric emptying". *Diseases of the Esophagus* 32 (2019): 1512.
9. M Konradsson., et al. "Diagnostic criteria and symptom grading for delayed gastric conduit emptying after esophagectomy for cancer: international expert consensus based on a modified Delphi process". *Diseases of the Esophagus* 33 (2020): 1177.
10. MKH Maus., et al. "Gastric Outlet Obstruction After Esophagectomy: Retrospective Analysis of the Effectiveness and Safety of Postoperative Endoscopic Pyloric Dilatation". *World Journal of Surgery* 40 (2016): 2405-2411.
11. Mohamed Abdelrahman., et al. "Randomised Controlled Trial (Feasibility study): of Prophylactic Balloon Dilatation During Ivor Lewis Esophagectomy to Prevent Delayed Gastric Emptying". *Acta Scientific Gastrointestinal Disorders* 6.8 (2023): 09-16.
12. D Dindo., et al. "Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey". *Annals of Surgery* 240 (2004): 205-213.

13. S Arya, *et al.* "The impact of pyloric drainage on clinical outcome following esophagectomy: a systematic review". *Diseases of the Esophagus* 28 (2015): 326-335.
14. HC Yang, *et al.* "Delayed Gastric Emptying after Esophagectomy: Management and Prevention". *Korean Journal of Thoracic and Cardiovascular Surgery* 53 (2020): 226-232.
15. JM Collard, *et al.* "Esophageal replacement: gastric tube or whole stomach?" *The Annals of Thoracic Surgery* 60 (1995): 261-267.
16. JP Pierie, *et al.* "The vascularization of a gastric tube as a substitute for the esophagus is affected by its diameter". *Diseases of the Esophagus* 11 (1998): 231-235.
17. JM Collard, *et al.* "The denervated stomach as an esophageal substitute is a contractile organ". *Annals of Surgery* 227 (1998): 33-39.
18. W Zhang, *et al.* "Gastric-tube versus whole-stomach esophagectomy for esophageal cancer: A systematic review and meta-analysis". *PLoS ONE* 12 (2017): e0173416.
19. L Barbera, *et al.* "[Effect of site and width of stomach tube after esophageal resection on gastric emptying]". *Zentralblatt fur Chirurgie* 119 (1994): 240-244.
20. JI Lee, *et al.* "A flow visualization model of gastric emptying in the intrathoracic stomach after esophagectomy". *The Annals of Thoracic Surgery* 91 (2011): 1039-1045.
21. RDL Akkerman, *et al.* "Surgical techniques to prevent delayed gastric emptying after esophagectomy with gastric interposition: a systematic review". *The Annals of Thoracic Surgery* 98 (2014): 1512-1519.
22. C Decker, *et al.* "Gastric emptying after esophagectomy: comparing single therapy versus dual therapy method for pyloric drainage". *Shanghai Chest* 4 (2020): 37.