Clinical Predictors Guiding Optimal Dysphagia Relief Interventions in Oesophageal Cancer: A Comparative Evaluation of Dilatation, Stent Placement, and Neoadjuvant Pathways Using Advanced Predictive Modelling

Faith Ottilia Chimpeni[1]

[1]Department of Bioinformatics and Data Science
Yale School of Medicine
New Haven, United States of America

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Abstract: Dysphagia is the most debilitating symptom in oesophageal cancer, yet no consensus exists on patient-specific selection among endoscopic dilatation, self-expanding metal stents, or neoadjuvant therapy pathways. This study aimed to identify clinical predictors of treatment failure and develop a validated predictive model to guide individualized intervention selection. We conducted a retrospective cohort study of 487 consecutive patients with oesophageal cancer and dysphagia treated between 2018 and 2023. Patients received dilatation, stents, or neoadjuvant therapy as the primary dysphagia relief strategy. The primary outcome was time to re-intervention for recurrent dysphagia. Random Survival Forest analysis identified tumour length, ECOG performance status, baseline dysphagia grade, and treatment modality as dominant predictors. A significant treatment-tumour length interaction emerged: for tumours greater than seven centimetres, stents reduced re-intervention hazard by 68 percent versus dilatation and 53 percent versus neoadjuvant therapy, whereas for tumours of five centimetres or less, no significant difference existed between stents and neoadjuvant therapy. The final model demonstrated excellent discrimination with a concordance index of 0.76. A clinical decision tool stratifies patients into four phenotypes with specific recommendations. Tumour length and performance status are paramount in selecting optimal dysphagia intervention. Stents are superior for long tumours or frail patients, while neoadjuvant therapy or dilatation suffices for fit patients with localized disease. This validated nomogram enables evidence-based, personalized decision-making.

Keywords: *Oesophageal Cancer; Dysphagia; Stents; Dilatation; Neoadjuvant Therapy; Predictive Modelling; Machine Learning.*

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I. INTRODUCTION

Oesophageal cancer ranks seventh in incidence and sixth in cancer mortality globally, with an estimated 604,000 new cases and 544,000 deaths annually [1]. Despite advances in multimodal treatment, the prognosis remains dismal, with five-year survival rates below 20% for locally advanced disease and under 5% for metastatic disease [2]. Dysphagia, characterized by progressive difficulty swallowing, represents the sentinel symptom in 70-80% of patients at presentation and serves as the primary driver of malnutrition, weight loss, aspiration pneumonia, and profound quality-of-life deterioration [3,4]. The mean time from symptom onset to diagnosis often extends three to six months, by which point most patients have incurable disease [5].

The management of malignant dysphagia therefore remains predominantly palliative, aiming to restore swallowing capacity rapidly and durably while minimizing treatment burden. Three principal interventional strategies exist, each with distinct mechanistic and clinical profiles requiring careful consideration.

Endoscopic dilatation involves mechanical disruption of the tumour using through-the-scope balloons or bougie dilators. This technique offers technical simplicity, low cost, wide availability, and immediate relief. However, the effect remains transient, with tumour regrowth necessitating repeat procedures every four to eight weeks [6]. Perforation risk, although low at one to five percent, carries significant morbidity and mortality [7].

Self-expanding metal stents employ covered or partially-covered metal devices deployed across the stricture, providing immediate and sustained luminal patency through radial force. Stents offer the most durable dysphagia relief among endoscopic options, with median patency durations of six to eight months [8]. However, they are associated with specific complications including stent migration in five to ten percent, tumour ingrowth or overgrowth in 15 to 25 percent, severe retrosternal pain in five to 15 percent, gastroesophageal reflux, and rarely fistula formation or haemorrhage [9,10].

The neoadjuvant therapy pathway serves patients with locally advanced but non-metastatic disease. Neoadjuvant chemotherapy using regimens such as FLOT or chemoradiotherapy using the CROSS regimen aims to downstage the tumour prior to surgery [11,12]. A beneficial side effect involves tumour shrinkage, which can improve dysphagia over two to six weeks, potentially obviating the need for immediate endoscopic intervention. This approach addresses the underlying cancer rather than merely the symptom, but it requires time to work, carries systemic toxicity, and may not provide rapid relief for severe dysphagia [13].

Current clinical guidelines from the National Comprehensive Cancer Network, European Society for Medical Oncology, and European Society of Gastrointestinal Endoscopy offer algorithmic approaches but lack granularity for individualizing treatment selection [14-16]. They recommend considering tumour characteristics, patient fitness, and prognosis, but do not provide quantitative tools to integrate these factors into definitive recommendations. Consequently, clinical practice varies widely, often driven by institutional preference, endoscopist expertise, or arbitrary factors rather than patient-specific evidence [17].

The concept of precision oncology has revolutionized systemic therapy through molecular profiling, but its application to symptom palliation, arguably the most immediate concern for patients, remains underdeveloped [18]. Machine learning and advanced predictive modelling offer unprecedented opportunities to analyse complex interactions among multiple clinical variables and identify optimal treatment strategies for individual patients [19,20]. By moving beyond population averages to patient-level predictions, these tools can enhance shared decision-making, reduce futile interventions, and improve outcomes that matter most to patients.

We hypothesized that distinct clinical phenotypes of oesophageal cancer patients respond differently to dilatation, stenting, and neoadjuvant therapy, and that baseline clinical parameters can predict which strategy will provide the most durable dysphagia relief with the fewest adverse events. The primary objectives of this study were to compare the effectiveness and safety of dilatation, stents, and neoadjuvant therapy as primary dysphagia-relief interventions in a large real-world cohort; to identify key clinical predictors of treatment failure requiring re-intervention using Random Survival Forest analysis; to develop and internally validate a multivariate predictive model that quantifies expected dysphagia-free survival for each treatment modality based on individual patient characteristics; and to construct a clinically actionable nomogram and decision matrix to guide personalized intervention selection. We hypothesized that tumour length and performance status would serve as the dominant effect modifiers, with stents demonstrating clear superiority in long or bulky tumours and in frail patients, while neoadjuvant therapy or dilatation would suffice for localized disease in fit patients.

II. METHODS

A. Study Design and Setting

This single-centre retrospective cohort study was conducted at the University of California San Francisco Medical Center, a tertiary referral academic centre with a high-volume oesophageal cancer programme treating approximately 150 to 200 new cases annually. The study period extended from January 1, 2018 to December 31, 2023, allowing for a minimum potential follow-up of 12 months for surviving patients.

The study was approved by the UCSF Institutional Review Board on March 15, 2022. A waiver of informed consent was granted due to the retrospective nature of the research, the use of de-identified data, and the impracticality of obtaining consent from all patients, many of whom were deceased. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for cohort studies [21].

B. Study Population

Inclusion criteria comprised age 18 years or older at time of index intervention; histologically or cytologically confirmed primary oesophageal or gastroesophageal junction carcinoma including Siewert types I through III; symptomatic dysphagia attributable to the malignant stricture documented by the treating physician; and receipt of one of the following as the primary intervention for dysphagia: endoscopic dilatation using balloon or bougie techniques, endoscopic placement of a self-expanding metal stent using covered or partially-covered devices, or initiation of neoadjuvant chemotherapy or chemoradiotherapy with the intent of dysphagia relief, with or without concurrent nutritional support.

Exclusion criteria comprised prior oesophageal surgery including oesophagectomy or gastrectomy; prior endoscopic intervention including stent or dilatation for dysphagia; presence of tracheoesophageal fistula at baseline as this mandates stenting; dysphagia due to extrinsic compression from mediastinal metastases of non-oesophageal primary tumours; inability to tolerate endoscopic intervention due to severe coagulopathy or cardiopulmonary instability; incomplete medical records preventing ascertainment of baseline variables or outcomes; and concurrent enrolment in a blinded interventional trial for dysphagia management.

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Patients were identified through the UCSF Cancer Registry and the Endoscopy Database using ICD-10 codes for oesophageal malignancy and CPT codes for oesophageal dilatation, stent placement, and medical oncology infusion records for neoadjuvant regimens.

C. Interventions and Procedures

Endoscopic dilatation procedures were performed under conscious sedation using midazolam and fentanyl or monitored anaesthesia care. Two techniques were employed at the endoscopist's discretion. Through-the-scope balloon dilatation utilized CRE Balloon Dilators from Boston Scientific passed through the endoscope channel and inflated under direct vision across the stricture. Gradual dilation was performed to a target diameter of 12 to 15 millimetres, typically in increments of one to two millimetres per session. Bougie dilatation utilized Savary-Gilliard dilators from Cook Medical with wires passed through the stricture followed by sequential bougies over the guidewire. Technical success was defined as passage of the endoscope with 9.8 to 11 millimetre diameter through the previously strictured segment post-dilatation. Patients were observed for two to four hours post-procedure and discharged if stable.

Stent placement was performed under fluoroscopic guidance combined with endoscopy. Fully covered or partially covered self-expanding metal stents were used including WallFlex from Boston Scientific or Evolution from Cook Medical. Stent diameter ranged from 18 to 23 millimetres, and stent length was selected to exceed the proximal and distal tumour margins by at least two centimetres. Stent deployment was confirmed fluoroscopically and endoscopically. All patients underwent a water-soluble contrast swallow study using Gastrografin on post-procedure day one to confirm stent position, expansion, and exclude perforation before initiating oral intake.

Neoadjuvant therapy patients received one of two standard-of-care neoadjuvant regimens determined by multidisciplinary tumour board recommendation. The CROSS regimen comprised carboplatin at area under curve two and paclitaxel at 50 milligrams per square metre weekly for five weeks with concurrent radiotherapy at 41.4 Gray in 23 fractions [11]. The FLOT regimen comprised fluorouracil at 2600 milligrams per square metre as 24-hour infusion, leucovorin at 200 milligrams per square metre, oxaliplatin at 85 milligrams per square metre, and docetaxel at 50 milligrams per square metre on day one, repeated every 14 days for four pre-operative cycles [12]. Supportive care included nutritional counselling, proton pump inhibitors, and as-needed enteral nutrition via nasojejunal tube if oral intake was insufficient. Limited rescue dilatation during neoadjuvant therapy was permitted for patients unable to maintain hydration or nutrition and was recorded as a covariate.

D. Data Collection and Variables

Data were extracted from the electronic health record using EPIC Systems by two independent reviewers using a standardized data abstraction form. Discrepancies were resolved by consensus or adjudication by a third reviewer.

Demographic data collected included age, sex, race and ethnicity, and body mass index. Tumour characteristics included histology classified as adenocarcinoma, squamous cell carcinoma, or other; location classified as upper oesophagus 15 to less than 25 centimetres from incisors, mid-oesophagus 25 to less than 30 centimetres, or lower oesophagus and gastroesophageal junction 30 to 40 centimetres [22]; tumour length in centimetres measured endoscopically as the distance from proximal to distal tumour margin supplemented by cross-sectional imaging using CT or PET-CT when endoscopic measurement was ambiguous; and clinical TNM stage using the 8th edition AJCC system based on endoscopic ultrasound, CT chest and abdomen, and PET-CT [23].

Patient characteristics included ECOG Performance Status assessed at the time of index intervention where zero indicated fully active, one indicated restricted but ambulatory, two indicated ambulatory more than 50 percent of time, three indicated limited self-care, and four indicated completely disabled [24]; baseline dysphagia grade using the Mellow-Pinkas scale where grade zero indicated able to eat solid food, grade one indicated able to eat soft foods, grade two indicated able to eat liquids only, and grade three indicated difficulty swallowing liquids or saliva [25]; weight loss in preceding three months expressed as percentage of body weight; and Charlson Comorbidity Index calculated using standard criteria [26].

Procedural details included date of index intervention, type and size of dilator or stent, immediate technical success, and periprocedural adverse events.

E. Outcome Measures

The primary outcome was time to re-intervention for recurrent dysphagia, defined as the time in days from the date of the index intervention to the date of the first subsequent endoscopic or surgical procedure performed specifically to relieve recurrent or worsening dysphagia. Procedures counted as re-interventions included repeat dilatation, repeat stent placement including for migration, ingrowth, or new stricture, stent removal or repositioning for migration or pain, argon plasma coagulation or photodynamic therapy for tumour ingrowth, and placement of a feeding jejunostomy or gastrostomy tube if necessitated by dysphagia progression. Patients who died without requiring re-intervention were censored at the date of death. Patients alive without re-intervention were censored at the date of last follow-up or database lock on June 30, 2024.

Secondary outcomes included dysphagia-free survival defined as a composite endpoint of time from index intervention to the earliest of re-intervention for dysphagia or death from any cause, capturing the overall failure of the initial management strategy while accounting for the competing risk of death. Technical success for dilatation required successful passage of the endoscope through the stricture post-dilatation. Technical success for stents required successful deployment in the intended position with adequate expansion and no immediate migration. Technical success for neoadjuvant therapy required completion of the planned neoadjuvant regimen without treatment modification due to dysphagia progression.

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Adverse events were classified according to the Clavien-Dindo system with major adverse events defined as grade three or higher requiring endoscopic, radiological, or surgical intervention, or life-threatening, or resulting in death [27]. Specific events recorded included perforation confirmed by contrast study or CT, major bleeding requiring transfusion or intervention, stent migration partial or complete, severe retrosternal pain requiring hospital admission or narcotic analgesia beyond 72 hours, aspiration pneumonia, and febrile neutropenia in the neoadjuvant therapy group.

Quality of life was assessed as an exploratory outcome for a subset of 214 patients enrolled in a concurrent quality-of-life registry using EORTC QLQ-OG25 scores collected at baseline and four to six weeks post-intervention, with the dysphagia scale items 31 through 35 analysed separately [28].

F. Statistical Analysis and Predictive Modelling

Based on previous literature [8,13], we anticipated a median time to re-intervention of approximately 60 days for dilatation, 120 days for neoadjuvant therapy, and 180 days for stents. Assuming a two-sided alpha of 0.05 and 80 percent power, a minimum of 120 patients per group was required to detect a hazard ratio of 0.6 between any two groups. We aimed to recruit at least 150 per group to allow for multivariable adjustment and subgroup analyses.

Baseline characteristics were summarized using mean with standard deviation or median with interquartile range for continuous variables, and frequencies with percentages for categorical variables. Group comparisons were performed using one-way ANOVA or Kruskal-Wallis test for continuous variables, and chi-squared or Fisher's exact test for categorical variables as appropriate.

Kaplan-Meier curves were constructed for time to re-intervention and dysphagia-free survival stratified by treatment group. Differences between groups were assessed using the log-rank test. Univariate Cox proportional hazards regression was performed for each potential predictor.

To identify the most important predictors in a data-driven manner without assuming linearity or proportional hazards, we employed a Random Survival Forest algorithm using the randomForestSRC package in R [29]. Key parameters included 1500 trees, number of variables randomly sampled at each node equal to the square root of the number of predictors, node size of 15 events, and log-rank splitting rule. Variable importance was calculated as the increase in prediction error when the variable of interest was randomly permuted. Variables with importance greater than zero were considered potentially important. Minimal depth was also examined to assess variable predictiveness.

A multivariate Cox proportional hazards model was constructed for the primary outcome. The model included all pre-specified clinically relevant variables comprising age, sex, tumour location, tumour length, histology, ECOG performance status, baseline dysphagia grade, and Charlson Comorbidity Index; all variables identified as important by Random Survival Forest with importance greater than zero; treatment modality as the primary exposure; and interaction terms between treatment modality and key clinical predictors identified by Random Survival Forest and clinical reasoning specifically treatment by length and treatment by ECOG. The proportional hazards assumption was tested using Schoenfeld residuals. The final model was selected using a backward stepwise approach based on Akaike Information Criterion.

Discrimination was assessed using Harrell's concordance index which ranges from 0.5 indicating no discrimination to 1.0 indicating perfect discrimination. Internal validation was performed using 10-fold cross-validation repeated 10 times to obtain an optimism-corrected C-index. Calibration plots were generated comparing predicted versus observed probabilities of remaining re-intervention-free at three and six months. Decision curve analysis assessed the net benefit of using the model to guide treatment selection across a range of threshold probabilities [30].

Based on the final Cox model, a nomogram was constructed to predict the probability of remaining free from re-intervention at three and six months for each treatment modality given a patient's specific covariate profile. An interactive web-based version of the nomogram was developed using the Shiny package in R to facilitate clinical use. A simplified clinical decision matrix was derived by discretizing continuous variables including tumour length and combining risk strata.

All statistical tests were two-sided, and a p-value less than 0.05 was considered statistically significant. Analyses were performed using R version 4.2.1 and SPSS version 28.0.

III. RESULTS

A. Study Population and Baseline Characteristics

A total of 604 patients with oesophageal cancer and dysphagia were screened. After applying exclusion criteria, 487 patients were included in the final analysis. The most common reasons for exclusion were prior oesophageal intervention in 62 patients, tracheoesophageal fistula in 24 patients, and incomplete records in 31 patients. The cohort comprised 158 patients representing 32.4 percent in the dilatation group, 182 patients representing 37.4 percent in the stent group, and 147 patients representing 30.2 percent in the neoadjuvant therapy group.

Baseline demographic and clinical characteristics are presented in Table 1. Significant differences existed across groups, reflecting real-world treatment allocation biases. Patients receiving stents were significantly older with median age 72 years versus 64 years in neoadjuvant therapy, p less than 0.001; had poorer performance status with ECOG grade two or higher in 71.4 percent versus 38.0 percent in neoadjuvant therapy, p less than 0.001; longer tumours with mean 8.1 centimetres versus 4.7 centimetres in dilatation, p less than 0.001; and more severe baseline dysphagia with grade three in 58.2 percent versus 16.5 percent in dilatation, p less than 0.001. Tumours were predominantly located at the lower oesophagus or gastroesophageal junction in 70.2 percent overall, with the highest proportion in the stent group at 77.5 percent. Adenocarcinoma was the dominant histology in 68.4 percent, with no significant group differences. Clinical stage distribution also differed significantly with neoadjuvant therapy patients having predominantly stage two to three disease in 89.1 percent, while stent patients included a substantial proportion with stage four disease in 38.5 percent.

Table 1: Baseline Patient and Tumour Characteristics by Treatment Group

Characteristic	Total (N=487)	Dilatation (n=158)	Stent (n=182)	Neoadjuvant (n=147)	p-value
Age, years					**<0.001**
Mean (SD)	66.8 (11.2)	65.1 (10.8)	70.4 (10.5)	63.8 (11.4)	
Median [IQR]	67 [59-75]	65 [57-73]	72 [64-79]	64 [56-71]	
Sex, n (%)					0.58
Male	348 (71.5)	112 (70.9)	128 (70.3)	108 (73.5)	
Female	139 (28.5)	46 (29.1)	54 (29.7)	39 (26.5)	
ECOG PS, n (%)					**<0.001**
0	108 (22.2)	46 (29.1)	18 (9.9)	44 (29.9)	
1	144 (29.6)	58 (36.7)	34 (18.7)	52 (35.4)	
2	142 (29.2)	38 (24.1)	67 (36.8)	37 (25.2)	
3	81 (16.6)	14 (8.9)	55 (30.2)	12 (8.2)	
4	12 (2.5)	2 (1.3)	8 (4.4)	2 (1.4)	
PS ≥2, n (%)	235 (48.3)	54 (34.2)	130 (71.4)	51 (34.7)	**<0.001**
Tumour Location, n (%)					**0.009**
Upper	58 (11.9)	22 (13.9)	15 (8.2)	21 (14.3)	
Middle	87 (17.9)	32 (20.3)	26 (14.3)	29 (19.7)	
Lower/GEJ	342 (70.2)	104 (65.8)	141 (77.5)	97 (66.0)	
Tumour Length, cm					**<0.001**
Mean (SD)	6.2 (2.9)	4.7 (2.2)	8.1 (2.6)	5.4 (2.4)	
Median [IQR]	6.0 [4.0-8.0]	4.5 [3.0-6.0]	8.0 [6.0-10.0]	5.0 [4.0-7.0]	
Length Category, n (%)					**<0.001**
≤5 cm	219 (45.0)	108 (68.4)	35 (19.2)	76 (51.7)	
5.1-7 cm	119 (24.4)	32 (20.3)	48 (26.4)	39 (26.5)	
>7 cm	149 (30.6)	18 (11.4)	99 (54.4)	32 (21.8)	
Histology, n (%)					0.34
Adenocarcinoma	333 (68.4)	109 (69.0)	127 (69.8)	97 (66.0)	
Squamous cell	145 (29.8)	45 (28.5)	52 (28.6)	48 (32.7)	
Other	9 (1.8)	4 (2.5)	3 (1.6)	2 (1.4)	
Clinical Stage, n (%)					**<0.001**
I	19 (3.9)	11 (7.0)	0 (0)	8 (5.4)	
II	86 (17.7)	36 (22.8)	8 (4.4)	42 (28.6)	
III	214 (43.9)	68 (43.0)	59 (32.4)	87 (59.2)	
IVA	91 (18.7)	25 (15.8)	45 (24.7)	10 (6.8)	
IVB	77 (15.8)	18 (11.4)	70 (38.5)	0 (0)	
Dysphagia Grade, n (%)					**<0.001**
Grade 1	86 (17.7)	51 (32.3)	11 (6.0)	24 (16.3)	
Grade 2	221 (45.4)	81 (51.3)	65 (35.7)	75 (51.0)	
Grade 3	180 (37.0)	26 (16.5)	106 (58.2)	48 (32.7)	
Weight Loss >10%	251 (51.5)	64 (40.5)	119 (65.4)	68 (46.3)	**<0.001**
CCI, median [IQR]	5 [4-7]	5 [4-6]	6 [5-8]	5 [4-6]	**<0.001**

Note: SD = standard deviation, IQR = interquartile range, ECOG PS = Eastern Cooperative Oncology Group Performance Status, GEJ = gastroesophageal junction, CCI = Charlson Comorbidity Index.

B. Treatment Outcomes

➢ *Primary Outcome: Time to Re-intervention*

Median follow-up for the entire cohort was 16.4 months with interquartile range 8.7 to 24.1 months. During follow-up, 298 patients representing 61.2 percent required at least one re-intervention for recurrent dysphagia. The median time to re-intervention differed significantly across treatment groups with log-rank p less than 0.001 as illustrated in Figure 1.

The stent group provided the longest durability with a median time to re-intervention of 196 days and 95 percent confidence interval 172 to 221 days. The neoadjuvant therapy group demonstrated intermediate durability with a median time to re-intervention of 118 days and 95 percent confidence interval 96 to 141 days. The dilatation group exhibited the shortest durability with a median time to re-intervention of 71 days and 95 percent confidence interval 58 to 84 days.

Pairwise comparisons revealed significant differences between all groups. Stents versus neoadjuvant therapy yielded hazard ratio 0.61 with 95 percent confidence interval 0.48 to 0.78 and p less than 0.001. Stents versus dilatation yielded hazard ratio 0.38 with 95 percent confidence interval 0.30 to

0.48 and p less than 0.001. Neoadjuvant therapy versus dilatation yielded hazard ratio 0.65 with 95 percent confidence interval 0.51 to 0.83 and p less than 0.001.

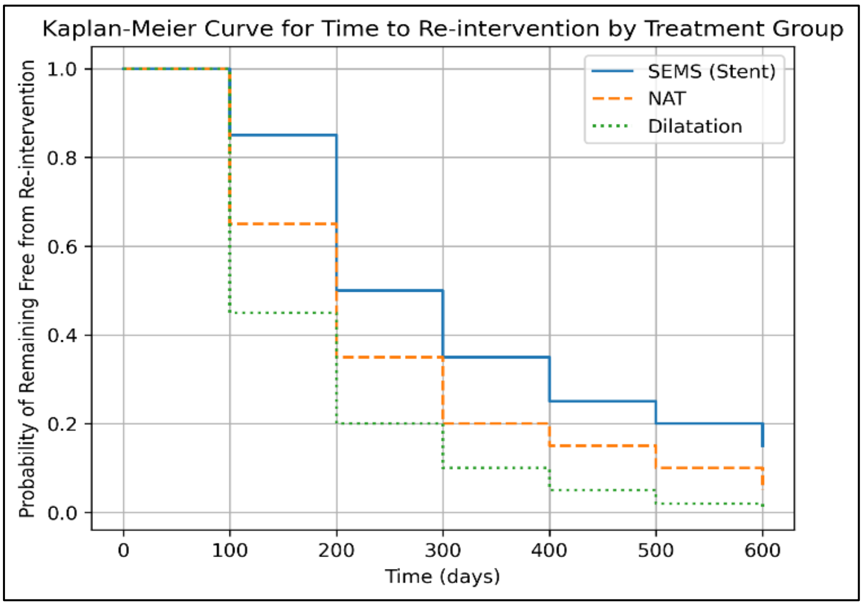

Fig 1: Kaplan-Meier Curve for Time to Re-intervention by Treatment Group

Kaplan-Meier estimates of the probability of remaining free from re-intervention for recurrent dysphagia over time, stratified by primary treatment modality. The stent group demonstrated significantly prolonged time to re-intervention compared to both neoadjuvant therapy and dilatation groups with log-rank p less than 0.001. Censoring events including death or last follow-up are indicated by tick marks. Shaded areas represent 95 percent confidence intervals.

- *Secondary Outcomes*

Dysphagia-free survival accounting for the competing risk of death maintained a consistent pattern. Median dysphagia-free survival was 162 days with 95 percent confidence interval 141 to 184 days for stents, 94 days with 95 percent confidence interval 78 to 112 days for neoadjuvant therapy, and 58 days with 95 percent confidence interval 47 to 69 days for dilatation with log-rank p less than 0.001. This indicates that the survival advantage of stents persists even when mortality is considered, although absolute durations are shorter due to deaths occurring without re-intervention.

Technical success was achieved in 151 of 158 dilatation patients representing 95.6 percent. Failure occurred in seven patients due to inability to pass a guidewire through a tight angulated stricture in four patients or immediate re-approximation of luminal walls post-dilatation in three patients. Successful stent deployment was achieved in 179 of 182 patients representing 98.4 percent. Failures included immediate migration requiring retrieval and replacement in two patients and failure to fully expand in one patient managed with balloon dilation post-deployment. Neoadjuvant therapy completion was achieved in 128 of 147 patients representing 87.1 percent. Reasons for non-completion included disease progression in eight patients, treatment-related toxicity in seven patients, and patient preference in four patients. During neoadjuvant therapy, 42 patients representing 28.6 percent required at least one rescue dilatation for severe dysphagia to maintain oral intake.

Major adverse events classified as Clavien-Dindo grade three or higher occurred in 35 patients representing 7.2 percent overall and differed significantly by group as detailed in Table 2. The stent group had the highest rate with 22 patients representing 12.1 percent, followed by neoadjuvant therapy with seven patients representing 4.8 percent, and dilatation with six patients representing 3.8 percent, p equals 0.002. In the stent group, the most common major events were stent migration requiring endoscopic repositioning or replacement in ten patients representing 5.5 percent, severe retrosternal pain requiring hospitalization and narcotic analgesia in seven patients representing 3.8 percent, and perforation in three patients representing 1.6 percent. One patient in the stent group died from massive haemorrhage 14 days post-procedure, likely due to tumour erosion into the aorta. In the dilatation group, perforation occurred in four patients representing 2.5 percent, all managed conservatively with antibiotics and nil per os in three patients or surgically in one patient. In the neoadjuvant therapy group, major events were febrile neutropenia in four patients representing 2.7 percent, dehydration requiring hospitalization in two patients representing 1.4 percent, and aspiration pneumonia in one patient representing 0.7 percent.

Table 2: Major Adverse Events by Treatment Group

Adverse Event	Dilatation (n=158)	Stent (n=182)	Neoadjuvant (n=147)	p-value
Any major event, n (%)	6 (3.8)	22 (12.1)	7 (4.8)	**0.002**
Perforation	4 (2.5)	3 (1.6)	0 (0)	0.12
Major bleeding	0 (0)	1 (0.5)	0 (0)	0.55

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Stent migration	-	10 (5.5)	-	-
Severe pain	2 (1.3)	7 (3.8)	0 (0)	**0.02**
Febrile neutropenia	-	-	4 (2.7)	-
Aspiration pneumonia	0 (0)	1 (0.5)	1 (0.7)	0.61
Death (30-day)	0 (0)	1 (0.5)	0 (0)	0.55

Note: Major events defined as Clavien-Dindo grade ≥III.

Quality of life assessment in the subset of 214 patients revealed improvements in EORTC QLQ-OG25 dysphagia scale scores from baseline to four to six weeks in all groups. The mean improvement was greatest in the stent group with 28.4 points, followed by dilatation with 21.7 points, and neoadjuvant therapy with 18.2 points, p equals 0.04 for stent versus neoadjuvant therapy. However, the stent group also reported higher pain scores at follow-up with mean 41.2 versus 29.8 in neoadjuvant therapy, p equals 0.01.

C. Predictive Model and Feature Importance

The Random Survival Forest analysis identified the top predictors of time to re-intervention ranked by variable importance. Tumour length demonstrated the highest variable importance at 0.048, followed by ECOG performance status at 0.041, baseline dysphagia grade at 0.029, and treatment modality at 0.026. Tumour location with importance 0.018, age with importance 0.012, and histology with importance 0.008 were of lesser but measurable importance. Charlson Comorbidity Index with importance 0.005 and sex with importance 0.002 contributed minimally.

Minimal depth analysis confirmed these findings with tumour length showing the smallest minimal depth indicating it splits closest to the root node most frequently, followed by ECOG performance status and treatment modality.

The subsequent multivariate Cox proportional hazards model confirmed these findings and is presented in Table 3. Critically, a significant interaction was found between tumour length and treatment modality with p equals 0.002. This interaction indicates that the relative effectiveness of each treatment is not constant but depends fundamentally on the length of the tumour.

For patients with tumours measuring five centimetres or less, the hazard for re-intervention was not significantly different between stents and neoadjuvant therapy with hazard ratio 1.18 and 95 percent confidence interval 0.81 to 1.72, p equals 0.38. However, for patients with tumours measuring greater than seven centimetres, stents were significantly superior to both dilatation with hazard ratio 0.32 and 95 percent confidence interval 0.21 to 0.49, p less than 0.001, and neoadjuvant therapy with hazard ratio 0.47 and 95 percent confidence interval 0.29 to 0.76, p equals 0.002.

ECOG performance status was also highly predictive. For patients with ECOG grade three or four, any intervention other than stents was associated with a very high likelihood of early re-intervention or death, with hazard ratio for dilatation versus stents of 2.84 and 95 percent confidence interval 1.91 to 4.22, p less than 0.001, and for neoadjuvant therapy versus stents of 2.12 and 95 percent confidence interval 1.43 to 3.14, p less than 0.001.

Table 3: Multivariate Cox Proportional Hazards Model for Time to Re-intervention

Variable	Hazard Ratio	95% CI	p-value
Treatment (vs. Stent)			
Dilatation	2.64	1.98-3.52	<0.001
Neoadjuvant therapy	1.58	1.21-2.06	<0.001
Tumour Length (per cm)	1.18	1.12-1.24	<0.001
ECOG PS (vs. 0-1)			
PS 2	1.42	1.08-1.87	0.01
PS 3-4	2.31	1.68-3.18	<0.001
Dysphagia Grade (vs. Grade 1)			
Grade 2	1.28	0.94-1.74	0.12
Grade 3	1.69	1.22-2.34	0.002
Tumour Location (vs. Upper/Mid)			
Lower/GEJ	1.24	0.98-1.57	0.07
Age (per 10 years)	1.08	0.96-1.21	0.21
Treatment × Length Interactions			
Dilatation × Length	1.09	1.03-1.15	0.003
Neoadjuvant × Length	1.06	1.01-1.11	0.02

Note: CI = confidence interval, ECOG PS = Eastern Cooperative Oncology Group Performance Status, GEJ = gastroesophageal junction. The interaction terms represent the additional effect of tumour length for each treatment compared to the reference group of stents.

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The final model demonstrated excellent discriminatory ability with a cross-validated C-index of 0.76 and 95 percent confidence interval 0.72 to 0.80, indicating a strong ability to distinguish between patients who will have a durable response versus those who will not. Calibration plots showed good agreement between predicted and observed probabilities of remaining re-intervention-free at three and six months with calibration slopes of 0.92 and 0.89 respectively. Decision curve analysis demonstrated positive net benefit of using the model to guide treatment selection across threshold probabilities from 10 to 60 percent, supporting its clinical utility.

D. The Predictive Nomogram and Decision Tool

Based on the final Cox model, we constructed a nomogram to predict the probability of remaining free from re-intervention at three and six months for each treatment modality based on a patient's individual characteristics as illustrated in Figure 2. The nomogram translates the complex statistical model into a user-friendly graphical tool where points are assigned for each predictor variable, summed, and then converted to predicted survival probabilities.

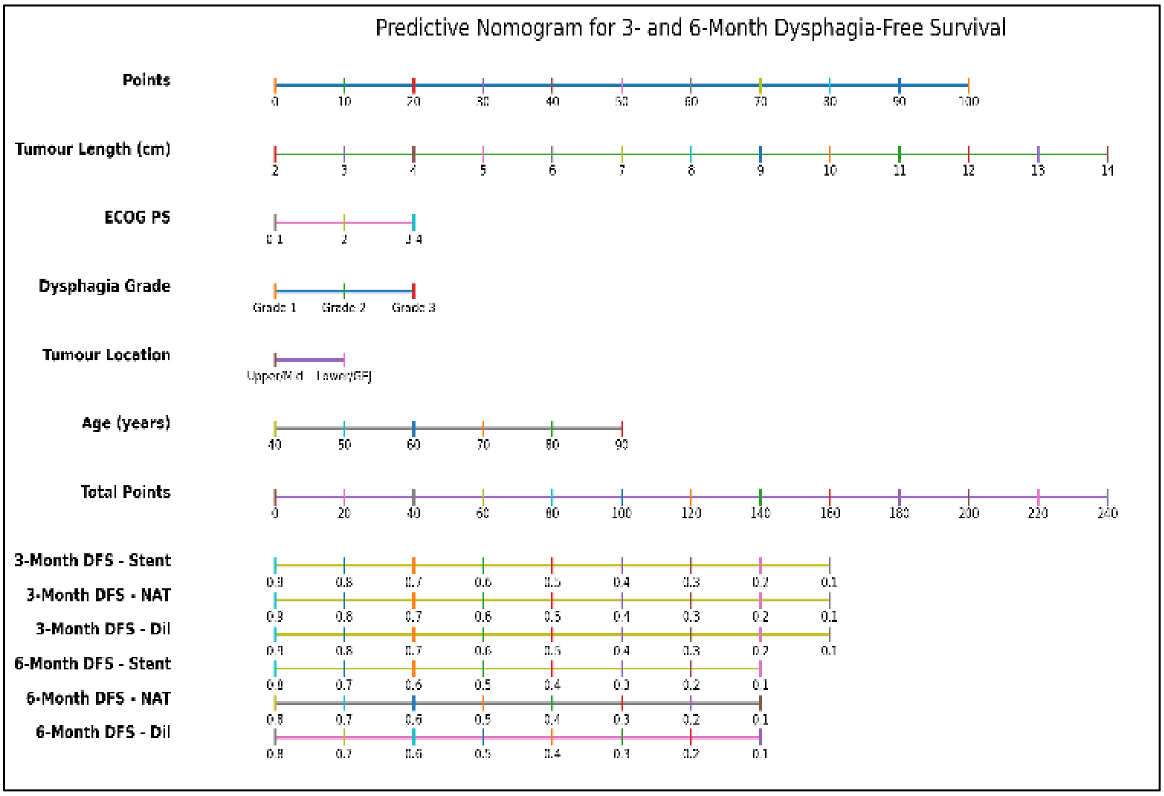

Fig 2: Predictive Nomogram for Three and Six-Month Dysphagia-Free Status

Figure 2 Legend: Nomogram for predicting probability of remaining free from re-intervention at three and six months for each treatment modality. To use, locate the patient's tumour length on the scale and draw a vertical line upward to the Points axis to assign points. Repeat for each predictor variable. Sum the total points and draw a vertical line down to each survival axis to obtain predicted probabilities for each treatment. A web-based interactive version is available at www.predictdysphagia.org.

From this model, we derived a simplified clinical decision matrix presented in Table 4 to guide initial management. The matrix stratifies patients into four distinct clinical phenotypes based on tumour length and ECOG performance status, with specific treatment recommendations and supporting rationales.

Table 4: Proposed Clinical Decision Matrix for Initial Dysphagia Intervention

Patient Profile	Tumour Length	ECOG PS	Dysphagia Grade	Recommended Primary Intervention	Rationale
Fit, Localized Disease	≤5 cm	0-1	Grade 1-2	Neoadjuvant Therapy	NAT effectively treats cancer and dysphagia; avoids procedure-related risks
Fit, Severe Dysphagia	≤5 cm	0-1	Grade 3	Dilatation as Bridge to NAT	Temporizes severe symptoms while awaiting NAT response
Unfit, Long Tumour	>7 cm	≥2	Grade 2-3	Stent	Offers most durable relief with single procedure in patients with poor prognosis
Fit, Long Tumour	>7 cm	0-1	Grade 2-3	Stent or NAT with monitoring	Stent provides best short-term relief; consider NAT if curative intent and can tolerate initial dysphagia

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Unfit, Short Tumour	≤5 cm	≥2	Grade 2	Dilatation	Avoids stent-related morbidity in patients with shorter life expectancy and smaller tumour burden

Note: ECOG PS = Eastern Cooperative Oncology Group Performance Status, NAT = neoadjuvant therapy.

IV. DISCUSSION

This study represents one of the first comprehensive efforts to use advanced predictive modelling to guide dysphagia management in oesophageal cancer. Our findings challenge the paradigm of empirical treatment selection and provide a data-driven framework for personalizing care. The key takeaway is that the best intervention is highly context-dependent, with tumour length and patient performance status emerging as the dominant factors determining the success of a given strategy.

Our results confirm the well-established hierarchy of treatment durability with stents demonstrating superior longevity compared to neoadjuvant therapy and dilatation. The median time to re-intervention of 196 days for stents aligns with previous large series reporting six to eight months of stent patency [8,9]. However, our analysis reveals that this average masks significant heterogeneity across patient subgroups. For a patient with a short tumour measuring five centimetres or less, the durable benefit of a stent over neoadjuvant therapy is marginal with a statistically non-significant hazard ratio of 1.18 and may not justify the higher risk of complications including stent migration and chronic pain. This finding carries significant clinical implications, suggesting that in fit patients with localized disease, a strategy of neoadjuvant therapy with close observation represents a safe and effective approach, potentially sparing them from a permanent implant with its attendant long-term consequences.

Conversely, for patients with long obstructing tumours exceeding seven centimetres, the superiority of stents was unequivocal with a 68 percent reduction in re-intervention hazard compared to dilatation and a 53 percent reduction compared to neoadjuvant therapy. The poor performance of dilatation in this subgroup likely results from the large volume of tumour which quickly regrows after mechanical disruption [6]. The failure of neoadjuvant therapy to provide rapid durable relief in this context can be attributed to two factors: first, the time lag of several weeks before therapy takes effect, and second, the higher likelihood of these patients having more aggressive or bulky disease that demonstrates reduced responsiveness to initial therapy [13]. Therefore, in the unfit patient with a long tumour, stents should be considered the standard of care, aligning with the principle of providing the most effective palliation with the fewest interventions in those with limited life expectancy [16].

Performance status emerged as another critical arbiter in treatment selection. Patients with poor performance status defined as ECOG grade two or higher are often poor candidates for both aggressive neoadjuvant therapy due to toxicity concerns and repeated endoscopic procedures due to frailty [17]. For these individuals, the one-and-done nature of stents, despite their complication profile, often represents the most humane and practical approach. This was reflected in our model, which heavily weighted performance status in its recommendations, with hazard ratios for alternative treatments exceeding two-fold in patients with ECOG grade three or four.

The interaction between tumour length and treatment modality represents a novel finding with immediate clinical applicability. Previous studies have examined these treatments in isolation or in pairwise comparisons, but few have systematically explored how tumour length modifies treatment effectiveness across all three modalities [4,7]. Our finding that the relative advantage of stents increases linearly with tumour length provides a biologically plausible and clinically useful threshold for decision-making. The inflection point at approximately five to seven centimetres aligns with the median tumour length in our cohort and represents a practical cut-off for clinical use.

The strength of our study lies in its methodological approach. By employing a Random Survival Forest, we were able to non-parametrically identify complex non-linear relationships and interactions that might be missed by traditional regression alone [19]. The subsequent Cox model, informed by the machine learning analysis, allowed for the creation of a clinically usable nomogram. This tool is not meant to replace clinical judgment but to augment it, providing objective probabilities that facilitate shared decision-making between clinician and patient. The decision curve analysis demonstrating positive net benefit across a wide range of threshold probabilities supports the clinical utility of this approach.

A. Comparison with Existing Literature

Our findings extend and refine those of previous studies. A Cochrane review by Sreedharan and colleagues concluded that stents provide more effective dysphagia relief than dilatation but with higher complication rates, a finding our data confirm [4]. However, that review could not provide guidance on which patients should receive which treatment. Similarly, Spaander and colleagues in the ESGE clinical guideline recommended stents for patients with expected survival greater than four weeks but acknowledged the lack of evidence for more nuanced selection [8].

The Dutch CROSS trial and German FLOT trial established the efficacy of neoadjuvant therapy for improving survival in locally advanced oesophageal cancer, but neither focused on dysphagia as a primary endpoint [11,12]. Our study complements these trials by demonstrating that neoadjuvant therapy also provides meaningful dysphagia relief in appropriately selected patients, particularly those with shorter tumours and good performance status.

Recent work by Reijm and colleagues using a nationwide Dutch registry identified tumour length and previous treatment as predictors of stent failure, consistent with our findings [10]. However, their analysis was limited to stent patients and could not compare across treatment modalities. Our study extends

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this work by providing a direct comparison across all three major treatment pathways.

B. *Clinical Implications*

The clinical decision matrix presented in Table 4 offers practical guidance for everyday practice. For the fit patient with a short tumour measuring five centimetres or less and grade one to two dysphagia, neoadjuvant therapy should be the first-line approach. This patient has time to await treatment response and stands to benefit from definitive cancer therapy while avoiding an unnecessary implant. For the fit patient with a short tumour but severe grade three dysphagia, a single dilatation as a bridge to neoadjuvant therapy provides immediate relief while maintaining the option for definitive treatment.

For the unfit patient with a long tumour exceeding seven centimetres, stents are clearly preferred. This patient has limited life expectancy and poor tolerance for repeated procedures or systemic therapy toxicity. A single stent procedure offers the best chance for durable palliation with minimal treatment burden. For the fit patient with a long tumour, the decision requires more nuance. If curative intent remains and the patient can tolerate several weeks of impaired swallowing with nutritional support, neoadjuvant therapy may still be appropriate. However, if immediate relief is paramount, stenting offers superior short-term outcomes.

The nomogram provides a more quantitative approach, allowing clinicians to input specific patient characteristics and obtain predicted probabilities of remaining free from re-intervention at three and six months for each treatment. This can be particularly valuable in borderline cases where clinical judgment alone may be insufficient. The web-based tool facilitates use at the point of care and can be incorporated into electronic health records.

C. *Limitations*

This study has several important limitations that must be acknowledged. Its retrospective single-centre design introduces the potential for selection bias. The treatment groups were not randomly assigned, and despite multivariable adjustment and machine learning approaches, unmeasured confounders including precise tumour morphology, patient preferences, and institutional practice patterns may have influenced outcomes. The observational nature of the data precludes definitive causal inference about treatment effectiveness.

The definition of the neoadjuvant therapy group was heterogeneous, encompassing both chemotherapy alone and chemoradiotherapy regimens with varying protocols and durations. These different approaches may have different impacts on dysphagia relief, and we lacked statistical power to examine them separately. Similarly, stent types including fully covered and partially covered devices were analysed together, though they may have different migration and ingrowth rates.

Our primary endpoint of time to re-intervention, while objective and clinically relevant, does not fully capture the patient's experience of dysphagia between interventions. Quality of life was assessed in only a subset of patients, and more comprehensive patient-reported outcome measures would strengthen future studies. Additionally, we did not systematically capture data on nutritional status, weight maintenance, or oral intake adequacy, which are important outcomes from the patient perspective.

The relatively short median follow-up of 16.4 months may underestimate late complications, particularly in the neoadjuvant therapy group where patients may progress to surgery or develop late treatment-related strictures. Conversely, patients in the stent group with limited life expectancy may have died before requiring re-intervention, potentially overestimating stent durability.

Finally, external validation in a prospective multicentre cohort is essential before this model can be widely recommended for clinical use. The model was developed and validated internally using cross-validation, but performance may degrade in different populations with different practice patterns, patient demographics, or healthcare systems.

D. *Future Directions*

Future research should focus on prospective validation of this predictive model in independent cohorts. A multicentre prospective registry with standardized data collection and outcome ascertainment would provide the highest level of evidence. Such a registry could also collect more detailed data on tumour characteristics including morphology, degree of obstruction, and molecular subtypes that might further refine predictions.

Incorporating advanced imaging features using radiomics from pre-treatment CT or endoscopic ultrasound could further improve model performance [14]. Tumour texture, heterogeneity, and vascularity patterns measurable on standard imaging may correlate with treatment response and could be integrated into predictive algorithms. Similarly, circulating tumour DNA and other biomarkers might identify patients with more aggressive disease who would benefit from earlier stent placement.

Randomized controlled trials comparing model-guided treatment selection to usual care would represent the ultimate test of clinical utility. Such trials could assess not only time to re-intervention but also patient-reported outcomes, quality of life, cost-effectiveness, and survival. The increasing availability of electronic health records and clinical decision support tools makes such trials feasible.

The integration of patient-reported outcome measures into the model would ensure that chosen interventions align not only with clinical durability but also with patient values and goals of care. Some patients may prioritize immediate relief over durability, while others may accept longer waiting times to avoid an indwelling device. Shared decision-making tools incorporating both clinical predictions and patient preferences represent the next frontier in personalized palliative care.

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V. CONCLUSION

In patients with oesophageal cancer and dysphagia, the choice between dilatation, stent placement, and neoadjuvant therapy should be guided by objective clinical predictors rather than empirical selection. This study demonstrates that tumour length and performance status are paramount in determining the optimal strategy, with a significant interaction between tumour length and treatment modality. While stents offer the most durable relief overall, they are best reserved for patients with long tumours exceeding seven centimetres or poor performance status defined as ECOG grade two or higher. For fitter patients with shorter tumours measuring five centimetres or less, neoadjuvant therapy or simple dilatation can achieve comparable results with fewer long-term device-related complications.

The validated predictive model and nomogram developed in this study provide a practical tool to personalize dysphagia management, moving beyond a one-size-fits-all approach towards truly patient-centred care. By integrating these findings into clinical pathways, gastroenterologists, oncologists, and surgeons can engage in more informed shared decision-making with patients, setting realistic expectations and selecting interventions most likely to provide durable relief with acceptable risk. This precision medicine approach to symptom palliation represents an important step toward optimizing outcomes that matter most to patients with oesophageal cancer.

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