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ORIGINAL ARTICLE – THORACIC ONCOLOGY

Enteral Feeding Access Has an Impact on Outcomes for Patients with Esophageal Cancer Undergoing Esophagectomy: An Analysis of SEER-Medicare

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ABSTRACT

Background. Optimal nutrition after esophagectomy is challenging due to alterations in eating, both from the tumor and during surgical recovery. Enteral nutrition via feeding tube is commonly used. The impact of feeding tubes on post-esophagectomy outcomes was examined in a large national data set.

Methods. Patients with esophageal cancer (1998–2013) undergoing esophagectomy were extracted from the Surveillance Epidemiology and End Results-Medicare database. Chi-square and *t* tests were used to compare categorical and continuous variables. Time trend analyses were performed with Cochran–Armitage survival using log-rank and multivariable analysis with generalized linear modeling.

Results. The study examined 2495 patients. The majority had enteral feeding access (71%, $n = 1794$) during the perioperative period. Mortality among the patients with feeding tubes was lower at 30 days (5.4% vs 8.4%), 60 days (9.0% vs 13.0%), and 90 days (12.2% vs 15.8%). In the multivariable analysis, the patients with feeding tubes had improved short-term survival at 30 days (odds ratio [OR], 0.65, 95% confidence interval [CI], 0.46–0.93), 60 days (OR, 0.64; 95% CI, 0.49–0.85), and 90 days (OR, 0.70; 95% CI, 0.54–0.90). The hospital stay was shorter for the patients undergoing enteral feeding tube placement (17.9 vs 19.5 days; $p = 0.04$). Discharge destination (home vs health care facility) showed no difference.

Conclusions. Feeding tubes in patients undergoing esophagectomy were associated with an increase in short-term survival up to 90 days after surgery. Feeding tube placement was not associated with higher rates of non-home discharges and did not prolong the hospital stay.

Achieving optimal nutrition for patients with esophageal cancer during the perioperative period is of paramount importance. Preoperatively, many patients experience dysphagia, especially those undergoing neoadjuvant treatment, making it difficult for them to maintain their baseline weight.[1] This phenomenon continues throughout the perioperative period. It is particularly challenging for these patients to maintain weight given the alterations from normal physiology that result from the esophageal resection and reconstruction during esophagectomy.

Numerous single-institution retrospective studies and several small randomized clinical trials have evaluated the utility of enteral feeding access for this patient population, but the results have been disparate.[2–16] The current study used a large national data set to further understand the impact of enteral feeding access on outcomes for patients undergoing esophagectomy for esophageal cancer. The study examined the impact of feeding tube placement on postoperative survival, but it also examined whether feeding tube placement is associated with adverse outcomes such as longer hospital stay or increased likelihood of discharge to a health care facility versus discharge to home.

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TABLE 1 Cohort selection

	Inclusion/exclusion criteria	Information from SEER-Medicare data	Cohort size
01	Esophageal and gastric cancer	Site recode ICD-O-3 (SITER1 = 150–155, 158, 159, 160–166, 168, 169)	93,949
02	First primary cancer only	Sequence no. (SEQ1 = 00, 01)	86,613
03	Year of cancer diagnosis from 1998 to 2013	Year of diagnosis (1998 ≤ YRDX1 ≤ 2013)	83,785
04	Age at diagnosis, 66+ years	Calculated using birth date and diagnosis date Medicare month of birth (BIRTHM), Medicare year of birth (BIRTHYR), diagnosis year (YRDX1), diagnosis months (MODX1)	64,402
		[(YRDX1-BIRTHYR) *12 + (MODX1-BIRTHM) + 1]/12 ≥ 66	
05	Histology confirmation (not on autopsy or death certificate)	Type of reporting source (SRC1 = 6, 7)	63,476
06	Exclude patients enrolled in Medicare for ESRD	Current reason for entitlement (CUR_ENT = 2, 3)	63,424
07	Medicare part A and B without HMO 1 year before and 1 year after diagnosis or until death	HMO indicators (gho1 = 0, not a member of HMO, one indicator for each month in the year)	40,551
		Entitlement indicators (mon1 = 3, part A and B, one indicator for each month in the tear)	
09	Identify surgery using ICD-9 procedure codes (MEDPAR)	4240, 4241, 4242, 4251, 4252, 4253, 4254, 4255, 4256, 4258, 4259, 4261, 4262, 4263, 4264, 4265, 4266, 4268, 4269—ICD-9 procedure codes	2922
10	Identify surgery using CPT codes (Carrier)	43110, 43115, 43119, 43120, 43107, 43108, 43112, 43113, 43116, 43117, 43118, 43121, 43122, 43123, 43124, 43289—CPT codes	4234
11	Surgery identified by both ICD-9 codes and CPT codes		2495

SEER Surveillance Epidemiology and End Results, *ICD* international classification of diseases, *ESRD* end-stage renal disease, *HMO* health maintenance organization, *MEDPAR* Medicare Provider Analysis and Review, *CPT* current procedural terminology

MATERIALS AND METHODS

Approval for this study and waiver of informed consent were obtained from the Carolinas Health Care System Institutional Review Board because the study was performed retrospectively with data rendered anonymous, thus presenting no patient risks.

Cohort Selection

The Surveillance Epidemiology and End Results (SEER)-Medicare-linked database was selected because it uniquely couples clinical data with claims information from a single payer for a group of non-selected patients. We queried the SEER-Medicare database for patients with gastroesophageal cancer, based on *International Classification of Diseases for Oncology*, 3rd ed (ICDO-3) site code, whose diagnosis was between 1998 and 2013.

Patients 66 years of age or older with a first primary esophageal cancer treated with esophagectomy were included in the study. Patients continuously enrolled in Medicare parts A and B without a health maintenance organization (HMO) for at least 1 year before and after diagnosis or until death were included. We excluded individuals receiving Medicare for end-stage renal disease.

Patients who underwent esophagectomy, as identified from claims data in the form of Current Procedural Terminology (CPT) codes (Table 1), were obtained from the Medicare Provider Analysis and Review (MEDPAR) file and Carrier file. The patients then were separated into groups on the basis of perioperative enteral feeding access in a similar fashion using CPT codes (43246, 43653, 43830, 44015, 44186, 44201, 44300, 44372, 49440, 49441, 56347). The cohort selection is seen in Table 1.

Variables of Interest

Patient factors and demographics such as age at diagnosis, gender, race, ethnicity, education quartile, Charlson Comorbidity Index, year of diagnosis, preoperative radiation, histology type, location of anastomosis, and staging information were obtained from the linked data sources. The codes used to identify the location of anastomosis, malnutrition, and staging information are found in Table 1.

Statistical Analysis

The primary outcomes of interest were mortality at defined time intervals, hospital length of stay, and discharge destination (home vs health care facility). The patient characteristics are summarized and presented in

TABLE 2 Patient demographics and univariate analyses

Variables	Overall cohort (n = 2495) n (%)	Enteral feeding access (n = 1794) n (%)	No enteral feeding access (n = 701) n (%)	p value
Characteristics				
Mean age (years)	73.0 ± 5.2	72.9 ± 5.1	73.1 ± 5.4	0.3092
Gender				0.0201
Male	1976 (79.2)	1442 (80.4)	534 (76.20)	
Female	519 (20.8)	352 (19.6)	167 (234.8)	
Race				0.2482
Caucasian	2287 (91.7)	1649 (91.9)	638 (91.0)	
Black	93 (3.7)	60 (3.3)	33 (4.7)	
Other	115 (4.6)	85 (4.8)	30 (4.3)	
Ethnicity				0.9714
Spanish–Hispanic–Latino	92 (3.7)	66 (3.7)	26 (3.7)	
Non-Spanish–Hispanic–Latino	2403 (96.3)	1728 (96.3)	675 (96.3)	
Education (missing = 11)				0.6240
Quartile 1 (lowest)	629 (25.3)	440 (24.7)	189 (27.0)	
Quartile 2	618 (24.9)	447 (25.1)	171 (24.4)	
Quartile 3	627 (25.2)	459 (25.7)	168 (24.0)	
Quartile 4 (highest)	610 (24.6)	438 (24.6)	172 (24.6)	
Charlson Comorbidity				0.2456
0	1381 (55.4)	994 (55.4)	387 (55.2)	
1	657 (26.3)	463 (25.8)	194 (27.7)	
2	283 (11.3)	201 (11.2)	82 (11.7)	
≥ 3	174 (7.0)	136 (7.6)	38 (5.4)	
Diagnosis year				< 0.0001
1998–2001	572 (22.9)	357 (19.9)	215 (30.7)	
2002–2005	751 (30.1)	514 (28.7)	237 (33.8)	
2006–2009	651 (26.1)	486 (27.1)	165 (23.5)	
2010–2013	521 (20.9)	437 (24.3)	84 (12.0)	
Anastomosis				< 0.0001
Abdominal	202 (8.0)	104 (5.8)	98 (14.0)	
Thoracic	872 (35.0)	533 (29.7)	339 (48.4)	
Cervical	1421 (57.0)	1157 (64.5)	264 (37.6)	
Histology type				0.2095
Adenocarcinoma	1951 (78.2)	1410 (78.6)	541 (77.2)	
Squamous	431 (17.3)	311 (17.3)	120 (17.1)	
Others	113 (4.5)	73 (4.1)	40 (5.7)	
T classification				0.0082
*T*is	55 (2.2)	29 (1.6)	26 (3.7)	
*T*1	719 (28.8)	513 (28.6)	206 (29.4)	
*T*2	397 (15.9)	276 (15.4)	121 (17.3)	
*T*3	1066 (42.7)	795 (44.3)	271 (38.7)	
*T*4	139 (5.6)	96 (5.4)	43 (6.1)	
*T*x	119 (4.8)	85 (4.7)	34 (4.8)	
N classification				0.1704
*N*0	1200 (48.1)	842 (46.9)	358 (51.1)	
*N*1	475 (19.0)	360 (20.1)	115 (16.4)	
*N*2	265 (10.6)	192 (10.7)	73 (10.4)	
*N*3	168 (6.8)	126 (7.0)	42 (6.0)	
*N*x	387 (15.5)	274 (15.3)	113 (16.1)	

TABLE 2 continued

Variables	Overall cohort (n = 2495) n (%)	Enteral feeding access (n = 1794) n (%)	No enteral feeding access (n = 701) n (%)	p value
M classification				0.1677
*M*0	2367 (94.9)	1708 (95.2)	659 (94.0)	
*M*1	63 (2.5)	46 (2.6)	17 (2.4)	
*M*x	65 (2.6)	40 (2.2)	25 (3.6)	
Neoadjuvant radiation				< 0.0001
Yes	994 (39.8)	786 (43.8)	208 (29.7)	
No	1501 (60.2)	1008 (56.2)	493 (70.3)	
Outcomes				
Mean hospital stay (days)	18.4 ± 17.0	17.9 ± 16.3	19.5 ± 18.5	0.0435
30-Day mortality	155 (6.2)	96 (5.4)	59 (8.4)	0.0044
60-Day mortality	252 (10.1)	161 (9.0)	91 (13.0)	0.0028
90-Day mortality	330 (13.2)	219 (12.2)	111 (15.8)	0.0162
Discharge destination				0.1027
Home	1685 (73.1)	1211 (72.2)	474 (75.6)	
Non-home	619 (26.9)	466 (27.8)	153 (24.4)	

Table 2. Chi-square and two-sided t tests were used to compare categorical and continuous variables based on enteral feeding access (significance level, $p = 0.05$).

The effect of covariates on mortality at 30, 60, and 90 days was assessed using multivariable logistic regression modeling with a logit link and stepwise selection (significance level of 0.15 for inclusion). A similar analysis was performed for effect of covariates on discharge destination, with exclusion of any patients who died during their hospital stay after the esophagectomy because these were considered to have other confounding variables that would limit generalizability. Analyses were performed with SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

The inclusion criteria were met by 2495 patients. The overall cohort had a mean age of 73 ± 5.2 years. The patients were largely male (79.2%) and Caucasian (91.7%). The majority presented with adenocarcinoma (78.2%). Fewer presented with squamous cell carcinoma (17.3%), and other histologies were diagnosed even less frequently (4.5%). Information regarding T, N, and M classification as well as other descriptive statistics is presented Table 2. Neoadjuvant radiation therapy was administered to 39.8% of the patients.

Enteral Feeding Access

Most of the patients had enteral feeding access in place (71.9%), which consisted of preoperative placement in 280 patients (11.2%), intraoperative placement in 1514 patients (60.9%), and postoperative placement in 22 patients (0.9%). Feeding tube placement varied by anastomotic location. Feeding tubes were most common with a cervical anastomosis (81.4%) followed by thoracic (61.1%) and abdominal (51.5%) anastomoses (Table 2). Additionally, feeding tube placement increased over time ($p < 0.01$). Multivariable regression identified year of diagnosis, anastomotic location, N classification, Charlson–Deyo Comorbidity Index, and neoadjuvant radiation as independent predictors of feeding tube placement (Table 3).

Demographics

In the univariate analysis, the patients with and without enteral feeding access differed significantly in terms of gender, year of diagnosis, location of anastomosis, T classification, and receipt of neoadjuvant radiation ($p < 0.05$ in each instance). The groups with and without enteral feeding access did not differ significantly in terms of age, race, ethnicity, education, Charlson Comorbidity Index, histology type, N classification, or M classification (Table 2).

Mortality

In the univariate analysis, the mortality rate for the patients who received a feeding tube was lower at 30 days (5.4% vs 8.4%), 60 days (9.0% vs 13.0%), and 90 days (12.2% vs 15.8%) ($p < 0.05$ in each instance; Table 2). In the multivariable analysis, the patients with enteral feeding access had improved survival at 30 days (odds ratio [OR],

TABLE 3 Multivariable analysis of covariate influence on enteral feeding access placement

Variables	Enteral feeding access (n = 1794) n (%)	OR (95% CI)	p value
Mean age (years)	72.9 ± 5.1	1.005 (0.987–1.024)	0.5895
Gender			0.1202
Female	352 (67.8)	1	
Male	1442 (73.0)	1.203 (0.953–1.518)	
Race			0.4609
Caucasian	1649 (72.1)	1	
Black	60 (64.5)	0.755 (0.458–1.245)	
Other	85 (73.9)	1.120 (0.703–1.784)	
Ethnicity			0.9487
Spanish–Hispanic–Latino	66 (71.7)	0.984 (0.594–1.629)	
Not Spanish–Hispanic–Latino	1728 (71.9)	1	
Education (missing = 11)			0.6147
Quartile 1 (lowest)	440 (70.0)	1.104 (0.839–1.454)	
Quartile 2	447 (72.3)	1.164 (0.889–1.524)	
Quartile 3	459 (73.2)	1.180 (0.902–1.543)	
Quartile 4 (highest)	438 (71.8)	1	
Charlson Comorbidity			0.0464
0	994 (72.0)	1	
1	463 (70.5)	0.888 (0.712–1.108)	
2	201 (71.0)	0.936 (0.689–1.270)	
≥3	136 (78.2)	1.636 (1.084–2.468)	
Diagnosis year			< 0.0001
1998–2001	357 (62.4)	0.323 (0.237–0.441)	
2002–2005	514 (68.4)	0.416 (0.308–0.563)	
2006–2009	486 (74.7)	0.572 (0.420–0.780)	
2010–2013	437 (83.9)	1	
Anastomosis			< 0.0001
Abdominal	104 (51.5)	1	
Thoracic	533 (61.1)	1.391 (1.006–1.923)	
Cervical	1157 (81.4)	4.493 (3.248–6.216)	
Histology type			0.7882
Adenocarcinoma	1410 (72.3)	1	
Squamous	311 (72.2)	1.031 (0.784–1.358)	
Others	73 (64.6)	0.869 (0.558–1.353)	
T classification			0.0933
*T*is	29 (52.7)	0.563 (0.274–1.159)	
*T*1	513 (71.4)	1.091 (0.699–1.703)	
*T*2	276 (69.5)	0.871 (0.550–1.378)	
*T*3	795 (74.6)	0.988 (0.649–1.506)	
*T*4	96 (69.1)	1.874 (0.868–4.044)	
*T*x	85 (71.4)	1	
N classification			0.0052
*N*0	842 (70.2)	1	
*N*1	360 (75.8)	1.434 (1.091–1.885)	
*N*2	192 (72.5)	1.540 (1.092–2.171)	
*N*3	126 (75.0)	1.802 (1.184–2.742)	
*N*x	274 (70.8)	0.953 (0.714–1.270)	

TABLE 3 continued

Variables	Enteral feeding access (n = 1794) n (%)	OR (95% CI)	p value
M classification			0.0893
*M*0	1708 (72.2)	1	
*M*1	46 (73.0)	0.732 (0.365–1.472)	
*M*x	40 (61.5)	0.413 (0.187–0.909)	
Neoadjuvant radiation			< 0.0001
Yes	1008 (67.2)	1.765 (1.417–2.199)	
No	786 (79.1)	1	

OR odds ratio, *CI* confidence interval

0.65; 95% confidence interval [CI], 0.46–0.93), 60 days (OR, 0.64; 95% CI, 0.49–0.85), and 90 days (OR, 0.70; 95% CI, 0.54–0.90) (Table 4).

Hospital Length of Stay

In the univariate analysis, the hospital stay was slightly shorter for the patients who underwent feeding tube placement (17.9 vs 19.5 days; p = 0.04, t test).

Discharge Destination

Age, gender, Charlson Comorbidity Index, histology type, and neoadjuvant radiation were found to predict discharge destination (home vs health care facility), whereas the presence of enteral feeding access did not (Table 5).

DISCUSSION

To our knowledge, this is the largest study to examine the impact of enteral feeding access on outcomes for patients with esophageal cancer who have undergone esophagectomy.

Feeding tubes were present in most of the study patients, either before or at the time of esophagectomy. Feeding tubes were more likely to be placed in individuals who had a higher incidence of comorbidities, those who were node positive, those undergoing neoadjuvant radiation, and those who had a cervical or thoracic anastomosis. These factors suggest that higher-risk patients are more likely to undergo jejunostomy tube placement. In addition, feeding tubes were more likely to be placed in patients with a more recent year of diagnosis.

The existing literature agrees on the importance of perioperative nutrition.[1–5,8,10,13,14,17–25] Most studies examining nutrition in esophagectomy patients typically assess the route of nutrition, the type of tube feeds used, and the timing of intervention. With regard to the route of nutrition, the preponderance of evidence supports enteral rather than parenteral feeding.[2,4,7,13,14,16,19,26,27] One study examining the route of enteral nutrition (e.g., jejunostomy, nasoenteric tubes) concluded that jejunostomy tubes provide the most benefit.[28]

More recently, reports describing feeding of post-esophagectomy patients by mouth as early as postoperative day 0 have emerged.[29,30] Although the data are promising, this approach has not reached widespread acceptance.

Several reports discourage the use of feeding tubes because of complications, lack of necessity, or increase in non-home discharge.[26,31] In a recent study by Choi et al.[32] 90% of their study population used a feeding tube at some time during the treatment, and 75% continued to use a feeding tube after discharge. In terms of complications, these authors report that the majority of the complications were minor in nature, such as cellulitis or dislodgement, managed most often at the bedside with minor interventions. However, 3% of their patients did require a return to the operating room for obstruction or hemorrhage. Other reports describe similar rates, which although justifying caution, are not prohibitive.[17,33–37]

In our series, the presence of enteral feeding access was not associated with an increased rate of non-home discharge or a longer hospital stay. Our data demonstrate a significant short-term survival advantage at 30, 60, and 90 days postoperatively for the patients who had enteral feeding access. Based on this finding, we recommend consideration of enteral feeding access in the form of a jejunostomy tube for all patients with esophageal cancer.

As with any similarly designed, nonrandomized, retrospective study using claims data, our study had limitations. There is inherent selection bias with surgeons choosing which patients receive enteral feeding access and which do not. Furthermore, data regarding actual use of enteral

TABLE 4 Multivariable analysis of mortality

Variables	30-day mortality		60-day mortality		90-day mortality	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	1.062 (1.032–1.093)	< 0.0001	1.063 (1.038–1.088)	< 0.0001	1.052 (1.029–1.075)	< 0.0001
Race (ref. white)						
Black						
Other						
Education (ref. Q1) (lowest)						
Quartile 2						
Quartile 3						
Quartile 4 (highest)						
Charlson Comorbidity (ref. 0)		0.0912		0.0170		0.0026
1	1.063 (0.710–1.591)		1.037 (0.751–1.434)		1.079 (0.810–1.437)	
2	1.423 (0.854–2.371)		1.299 (0.857–1.969)		1.406 (0.972–2.034)	
≥3	1.950 (1.108–3.434)		2.035 (1.287–3.219)		2.114 (1.396–3.200)	
Diagnosis year (ref. 2010–2013)		0.0948				
1998–2001	1.654 (0.951–2.877)					
2002–2005	1.752 (1.035–2.967)					
2006–2009	1.164 (0.658–2.060)					
Histology type (ref. adenocarcinoma)		0.0107		0.0002		< 0.0001
Squamous	1.771 (1.206–2.600)		1.946 (1.414–2.678)		1.903 (1.427–2.539)	
Others	1.553 (0.745–3.237)		0.895 (0.436–1.837)		1.446 (0.831–2.516)	
T classification (ref. T4)		00209		0.0850		0.0132
*T*is	0.276 (0.076–1.006)		0.444 (0.154–1.285)		0.362 (0.135–0.970)	
*T*1	0.400 (0.224–0.716)		0.479 (0.282–0.815)		0.408 (0.251–0.663)	
*T*2	0.441 (0.236–0.826)		0.487 (0.279–0.851)		0.499 (0.304–0.819)	
*T*3	0.395 (0.226–0.692)		0.536 (0.333–0.863)		0.509 (0.332–0.781)	
*T*X	0.285 (0.102–0.796)		0.369 (0.161–0.848)		0.404 (0.200–0.817)	
N classification (ref. *N*0)				0.0147		0.0191
*N*1			1.033 (0.700–1.526)		1.141 (0.813–1.602)	
*N*2			1.688 (1.085–2.625)		1.756 (1.178–2.615)	
*N*3			2.070 (1.258–3.407)		1.793 (1.116–2.881)	
*N*x			1.324 (0.888–1.976)		1.361 (0.953–1.944)	
Neoadjuvant radiation						0.1294
Yes versus no					1.231 (0.941–1.611)	
Operative feeding tube		0.0165		0.0020		0.0062
Yes versus no	0.654 (0.462–0.925)		0.642 (0.485–0.850)		0.699 (0.541–0.903)	

All blank cells in this table indicate covariates that did not reach a level of 0.15 in stepwise selection and hence were not included in the model

OR odds ratio, *CI* confidence interval

access for feeding and other details regarding enteral nutrition (e.g., formula, rates) are not available. Nonetheless, the study results contribute meaningful information to the conversation concerning the management of perioperative nutrition for patients with esophageal cancer. Additional limitations of this study included a population limited to patients 65 years or age or older, lack of knowledge about the indication for feeding tube placement, and other limitations common to administrative data sets.

CONCLUSIONS

Although debate exists in the literature as to the type and route of nutrition in esophagectomy patients during the perioperative period, it is well accepted that nutritional optimization remains an important issue. With this large data set, we demonstrated that enteral feeding access is associated with improved short-term survival and does not lengthen the hospital stay or increase the likelihood of a

TABLE 5 Multivariable analysis of covariate influence on discharge to home

Variables	Discharge to home	
	OR (95% CI)	p value
Age	0.928 (0.912–0.944)	< 0.0001
Gender		0.0022
Male versus female	1.401 (1.130–1.739)	
Charlson Comorbidity (ref. 0)		< 0.0001
1	0.713 (0.580–0.877)	
2	0.639 (0.484–0.843)	
≥ 3	0.331 (0.238–0.462)	
N classification (ref. N0)		0.0471
*N*1	0.841 (0.665–1.063)	
*N*2	0.856 (0.636–1.063)	
*N*3	1.482 (1.001–2.194)	
*N*x	0.827 (0.640–1.069)	
Histology type (ref. adenocarcinoma)		< 0.0001
Squamous	0.581 (0.461–0.733)	
Others	0.577 (0.386–0.864)	
Neoadjuvant radiation		0.0425
Yes versus no	1.218 (1.007–1.473)	

OR odds ratio, *CI* confidence interval

non-home discharge. We believe that careful consideration should be given to establishing enteral feeding access to maximize outcomes for these patients.

DISCLOSURE There are no conflicts of interest.

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