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# Computed tomography enterography predicts surgical-free survival in symptomatic stricturing Crohn's disease

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Received: 30 March 2022 / Revised: 9 June 2022 / Accepted: 9 June 2022 / Published online: 27 July 2022 © The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

## Abstract

**Objectives** The study aimed to predict surgical risks for patients with symptomatic stricturing Crohn's disease (CD) using computed tomography enterography (CTE) and to assess the association between CTE findings and pathological changes. **Methods** Crohn's disease patients with symptomatic stricture(s) were included. Exclusion criteria were concomitant penetrating disease, intra-abdominal abscess, previous bowel resection, or asymptomatic. Patients from January 2016 to December 2019 were identified as the primary cohort and those from January 2020 to June 2020 were identified as the validation cohort. Two independent experienced radiologists evaluated CTE variables including mucosal enhancement, mural stratification, wall enhancement, comb sign, lymphadenopathy, thick non-enhancing wall, bowel wall thickness, luminal diameter, and upstream lumen. Receiver operating characteristic, logistic regression, and nomogram were performed to identify the independent predictors of surgical-free survival. Histopathological scores of surgical specimens were also evaluated.

**Results** 198 patients (primary cohort, 123 with surgery and 75 under non-surgical intervention, and 41 patients (validation cohort) were analyzed. Bowel wall thickness < 5.9 mm, luminal stenosis > 3.35 mm, and upstream lumen < 27.5 mm were predictors of surgical-free survival for symptomatic stricturing CD patients. Logistic analysis showed the three CTE variables were the independent predictors of surgical-free survival (p < 0.001). A nomogram was developed with the concordance indexes of 0.905 and 0.892 in the primary and validation cohorts. Histopathological analysis showed bowel wall muscular hyperplasia/hypertrophy significantly correlated with luminal stenosis (r = -0.655, p = 0.008) and combined CTE variable (r = -0.683, p = 0.005).

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**Conclusions** CTE is highly predictive of disease course and surgical-free survival for patients with symptomatic stricturing CD, suggesting the important role of CTE in decision-making of treatment.

### **Graphical abstract**

Nomogram for CTE Variables to Predicts Surgical-free Survival in Symptomatic Stricturing Crohn's Disease				
Points 0 10 20 30 40 50 60 70	<sup>80</sup> 90 100 Independent predictors for surgical-free survival:			
Luminal	• Luminal diameter of >3.35 mm			
diameter, mm 1 2 3 4 5 6 7	(OR 20.92, 95% CI, 6.70-65.29, p<0.001)			
Upstream lumen, mm 70 65 60 55 50 45 40 35 30 3	• Upstream lumen of <27.5 mm			
Bowel wall thickness, mm	(OR 4.57, 95% CI, 1.61-12.98, p=0.004)			
Total points	• Bowel wall thickness of <5.9 mm			
Probability of Surgical-free Survival 0.05 0.25 0.75	(OR 3.63, 95% CI, 1.53-8.65, p=0.004)			
Duan M et al; 2022 DOI:	Abdominal Radiology The Official Journal of the Society of Abdominal Radiology wrww.abdominalradiology.org			

Keywords Crohn disease · Computed tomography · Surgery · ROC curve

#### Abbreviations

AUC	Area under curve
CTE	Computed tomography enterography
C-index	Concordance index
CI	Confidence interval
CD	Crohn's disease
DCA	Decision curve analysis
HBI	Harvey-Bradshaw index
IBD	Inflammatory bowel disease
PMTS	Possible maximum total score
ROC	Receiver operating characteristic

## Introduction

Stricturing Crohn's disease (CD) ultimately affects more than 50% of CD patients during lifetime [1]. Although tremendous advances in CD drug development have been gained, these established treatments are primarily for reducing inflammation rather than reversing fibrosis [2, 3]. Therefore, stricturing CD is usually treated with invasive methods [4]. However, it is challenging to determine appropriate timing of surgical intervention for symptomatic stricturing CD patients [5].

Early surgery is associated with fewer complications and lower recurrence in stenosing CD patients [6]. However, this is not absolute. Theoretically, symptomatic obstruction results from CD-associated strictures which are initially thought to be inflammatory and then develop to fibrostenosing phenotype [6, 7]. Whereas, data reveal that anti-tumor necrosis factors(anti-TNFs) may be efficacious for maintaining clinical remission and avoiding intestinal resection for years in stricturing CD [8], suggesting that medication can be an alternative to surgery in a group of patients with symptomatic stricturing CD. However, CD-associated intestinal fibrosis is currently irreversible, and surgical intervention is usually inevitable [9].

Although cross-sectional imaging allows characterization of the bowel wall composition [10], no reliable method can accurately assess the degree of inflammation and co-existing fibrosis in strictures noninvasively [5, 7]. Researchers had explored the relationship between Computed Tomography Enterography (CTE) and surgical pathology of the resected bowel in CD but failed to reliably differentiate between inflammatory and fibrostenotic lesions [11, 12]. The possible reason might be the heterogeneous definitions of fibrosis in histologic scoring systems among different studies [13]. In 2017, the study with a novel histological grading scheme indicated that the main histological changes of Crohn's fibrostenosing bowel strictures were the irreversible smooth muscle hyperplasia/ hypertrophy of bowel wall [14]. Therefore, we conducted this study to identify whether CTE parameters could predict surgical-free survival in symptomatic stricturing CD

and correlate with histological features of resected narrow bowel.

# **Material and methods**

## Patients

The retrospective study was conducted at the inflammatory bowel disease (IBD) center, department of general surgery, a tertiary Hospital. CD patients with obstructive symptoms were screened via a prospectively maintained database from January 2016 to June 2020 containing clinical manifestations, medical treatments, radiologic reports, etc. Patients with CTE examination indicating stricturing CD were included in our study. Patients with concomitant penetrating disease (n=99), intra-abdominal abscess (n=49), previous bowel resection (n = 86), asymptomatic bowel stricture (n = 152), incomplete CTE information (n = 34), and less than 1 year follow-up (n=28) were excluded. The following information was collected from the database: gender, disease duration at the time of CTE scanning, body mass index, Montreal classification [15], parenteral manifestations, smoking history, Harvey-Bradshaw index (HBI) [16], medical treatment after CTE. Patients from January 2016 to December 2019 were identified as the primary cohort and those from January 2020 to June 2020 were identified as the validation cohort. This study was approved by the ethics committee of our hospital (2021NZKY001).

#### Definitions and clinical management of CD patients

The diagnosis of CD was made based on the comprehensive results of endoscopic, histological, and/or radiological findings [6]. Stricturing disease was defined as at least 50% of luminal narrowing in the presence of radiological signs of CD as described by the radiologist [4]. Clinical management and decision for surgery were discussed and determined at a multidisciplinary team including gastroenterologists, radiologists, and surgeons. Then, patients receiving surgical interventions including bowel resection and/or stricture plasty for symptomatic stricture were included in surgical group. Those treated successfully with medication without clinical relapse within 1 year after CTE scanning were considered in non-surgical group.

## **CTE protocol**

All patients were given a liquid diet and took laxatives (Duphalac, 667 mg/mL lactulose, Abbott) to clean the intestines on the day before the CTE examination. Then, they were fasted for 6–8 h before the scan (water is permissible). All patients ingested 2000 mL isomatic mannitol solution (500 mL hyperosmotic mannitol solution plus 1500 mL water) over 60 min to ensure adequate distension of the small bowel. To reduce the artifacts arising from gastrointestinal peristalsis, raceanisodamine hydrochloride injection (10 mg) was intravenously administered 10 min before the CTE examination.

Following the unenhanced scan for the whole abdomen, iodinated contrast agent (ioversol, 300 mg/mL, GE Healthcare, Buckinghamshire, England) was injected intravenously by using a power injector (Ulrich, Medical, Missouri, USA). The infusion volume was 1.5 mL/kg and the flow rate was 3-4 mL/s. The arterial phase series was obtained with a post-injection delay of 30 s, and portal-venous phase was commenced at 30 s after arterial phase scan. The parameters for abdomen CT (Siemens, Munich, Germany) were as follows: 120 kV tube voltage, 230 mA tube current (with caredose 4D), 1/1 mm section thickness, 35–50 cm field of view,  $512 \times 512$  matrix, 0.5 s rotation time, and 1.2 pitch.

#### **Imaging analysis**

All CTE examinations were reviewed by 2 independent experienced radiologists (with 10 years and 15 years experiences) who were blinded to clinical data and pathological findings according to the CTE scoring system (Table 1 SuppInfo and Fig.\_1\_SuppInfo) [7, 11]. When multiple strictures were present, the radiologists selected the dominant one involved with clinical obstructive symptom(s) based on the greatest wall thickness, narrowest lumen, and the greatest difference between the luminal and prestenotic caliber. The CTE variables included mucosal enhancement (enhancement of mucosal that was superior in Hounsfield units to the adjacent, normal-appearing bowel segment), mural stratification (the differential enhancement of bowel wall layers), wall enhancement (enhancement of bowel wall that was superior in Hounsfield units to the adjacent, normal-appearing bowel segment), comb sign (segmental dilation or engorgement of vasa recta), lymphadenopathy (larger and/or enhancing more than their normal counterparts), thick non-enhancing wall (thick, homogeneous bowel wall with attenuation similar to adjacent, non-involved bowel segments), bowel wall thickness, luminal diameter, and upstream lumen [11].

#### Surgical pathology

Surgical specimens of 15 patients were collected prospectively for histopathological examinations. For each case, formalin-fixed, paraffin-embedded tissue sections from maximal narrowing and resection margin (relatively normal intestine) were stained with hematoxylin–eosin and masson trichrome. Then, the most 2–3 representative sections were reviewed and evaluated by an independent gastrointestinal pathologist (with 15 years experiences), who was blinded to the imaging findings, for the degree of active and chronic inflammation, fibrosis, muscular hyperplasia/hypertrophy, and space volume expansion separately to each mural layer. Thirdly, the total score for each category in each layer was obtained by calculating the sum of the scores of all components under that category. And a global score of each category for the whole bowel wall was then calculated as the sum of the scores of the particular category in each layer. These scores were further adjusted for comparison by calculating its percentage of the possible maximum total score (PMTS) (Table\_2\_SuppInfo) [14].

#### **Statistical analysis**

Statistical analysis was performed using IBM SPSS 23.0 software (IBM, Armonk, NY) and the rms package 16 in R version 4.0.3. Differences between groups were tested with the Chi-Square Test or the Mann–Whitney U test or Student's *t tests* based on data type and the normality of the data. Receiver operating characteristic (ROC) curve analysis was used for assessing the predictive value of continuous CTE variables for surgical-free survival. Univariate and multiple logistic regression analysis were performed to identify the independent factors of surgical-free survival. A combined CTE variable was calculated according to the results of the logistic regression of three continuous CTE variables (bowel wall thickness, luminal diameter, and upstream lumen) for surgical-free survival.

Then, a nomogram model was formulated. The concordance index(C-index) was calculated, and the calibration plots (1,000 bootstrap resamples) were established to compare nomogram-predicted versus actual probability of surgicalfree survival in both the primary and validation cohorts. Decision curve analysis (DCA) showing the net benefit (NB) of different threshold probability was performed to evaluate the potential ability of the predictive model to improve clinical decision-making [17, 18].

Finally, the relationship between CTE and pathological parameters was analyzed using spearman rank correlation. All analyses were two-tailed, and p < 0.05 was considered significant.

#### Results

#### **Patient demographics**

Of the 687 total CD patients screened, 448 patients were excluded from this study (Fig.\_2\_SuppInfo). Between January 2016 and December 2019, 198 CD patients were identified as primary cohort and 41 patients treated from January 2020 to June 2020 were identified as validation cohort (Table 1). In the primary cohort, the demographics

statistics between the surgical (n = 123) and non-surgical group (n = 75) were comparable. The HBI of surgical group was significantly higher than that of non-surgical group  $(8.3 \pm 0.2 \text{ vs } 7.8 \pm 0.2, p = 0.02)$ . After CTE examination, disease was induced to remission and maintaining therapy was started. 44(22.2%) patients were on biologics therapy with or without azathioprine, 94 (47.5%) with oral immunomodulator, and 60(30.3%) taking 5-aminosalicylic acids. Median follow-up for those with non-surgical intervention was 93.9 weeks (range 52-380 weeks). In surgical group, 30 (24.4%), 75 (61.0%), and 104 (84.6%) patients received surgery in 4, 12, and 26 weeks after CTE examination, respectively. The time between CTE and surgery in surgical group was  $16.8 \pm 1.0$  weeks. 70 (56.9%) patients received bowel resection and anastomosis and 53 (43.1%) underwent enterostomy. 25 (20.3%) patients underwent additional strictureplasties. No death was observed.

## Univariate analysis of CTE parameters in predicting successful medical treatment in symptomatic stricturing CD and ROC curve analysis

As shown in Table 2, CTE variables including mucosal enhancement, mural stratification, wall enhancement, comb sign, lymphadenopathy, and thick non-enhancing wall were not related with surgical-free survival in CD patients (P > 0.05). In contrast, bowel wall thickness and luminal diameter at the stricture, upstream lumen, and fibrostenosis score were strongly associated with surgical-free survival in univariate analysis. As shown in Fig. 1, ROC curve showed that wall thickness < 5.90 mm [area under curve (AUC) 0.80, 95% confidence interval (CI) 0.73–0.87, p < 0.001], upstream lumen < 27.50 mm (AUC 0.82, 95% CI 0.75–0.87, p < 0.001), and luminal diameter > 3.35 mm (AUC 0.87, 95%) CI 0.82–0.92, p < 0.001) were predictors of surgical-free survival in symptomatic stricturing CD patients. Furthermore, the combined CTE variable was calculated according to the results of the logistic regression as [0.73×luminal diameter  $-0.112 \times$  upstream lumen  $-0.248 \times$  wall thickness] / 0.73. It could further improve the AUC with the cutoff value of -2.9566 (sensitivity 93.3%, specificity 79.7%, AUC 0.905, 95% CI 0.762–0.923, P<0.001), which was significantly different from that of 3 single factors p < 0.05).

## Multiple logistic regression and its visualization by nomogram

In multiple analysis, the independent predictors for surgical-free survival were bowel wall thickness of < 5.9 mm [odds ratio (OR) 3.63, 95% CI 1.53–8.65, p = 0.004], luminal diameter of > 3.35 mm (OR 20.92, 95% CI 6.70–65.29, p < 0.001), and upstream lumen of < 27.5 mm (OR 4.57, 95% CI 1.61–12.98, p = 0.004). The combined CTE variable Table 1Demographic and<br/>clinical characteristics of<br/>surgical group and non-<br/>surgical group in symptomatic<br/>stricturing Crohn's disease<br/>patients (primary and validation<br/>cohorts)

Variables	Primary cohort		р	Validation cohort	
	Surgical group Non-surgical group				
Total	n=123	n=75		n=41	
Male	83	49	0.756	31	
Disease duration at the time of CTE scanning, weeks	$85.6 \pm 7.6$	$100.7 \pm 15.6$	0.342	$112.1 \pm 22.6$	
Body mass index, kg/m <sup>2</sup>	$18.1 \pm 0.3$	$25.0 \pm 4.5$	0.06	$17.7 \pm 1.0$	
Montreal classification					
Age, years			0.16		
A1 (≤16)	3	3		2	
A2 (17–40)	64	48		22	
A3 (>40)	56	24		17	
Disease location			0.165		
Ileal	58	43		31	
Ileocolonic	65	32		10	
Upper gastrointestinal	6	11	0.818	4	
Perianal lesions	22	26	0.192	12	
Parenteral manifestations	3	3	0.534	2	
Harvey–Bradshaw index	$8.3 \pm 0.2$	$7.8 \pm 0.2$	0.02	$8.0 \pm 0.3$	
Smoking history	23	9	0.214	5	
Medical treatment after CTE			0.435		
5-aminosalicylic acids	37	23		11	
Immunomodulator	62	32		17	
Biologics	24	20		13	

Results are expressed as n or mean  $\pm$  SEM

SEM standard error of the mean, CTE computed tomography enterography

Table 2	Univariate and multiple	logistic regression a	analysis of CTE	parameters in p	redicting successfu	Il medical treatment	in symptomatic stric-
turing C	Crohn's disease patients						

Variables	Univariate analysis			Multivariate logistic regression		
	Surgical group	Non-surgical group	р	OR	95% CI	р
Mucosal enhancement (mild to moderate vs severe)	14 (11.4%)	10 (13.3%)	0.44			
Mural stratification (mild to moderate vs severe)	5 (4.1%)	4 (5.3%)	0.53			
Wall enhancement (mild to moderate vs severe)	4 (3.3%)	3 (4.0%)	0.65			
Comb sign (mild to moderate vs severe)	5 (4.1%)	5 (6.7%)	0.30			
Lymphadenopathy	13 (10.6%)	11 (14.7%)	0.81			
Inflammation score (mild to moderate vs severe)	36 (29.3%)	22 (29.3%)	0.51			
Thick non-enhancing wall	30 (24.4%)	19 (25.3%)	0.32			
Wall thickness ( $\geq$ 5.9 mm vs < 5.9 mm)	24 (19.5%)	51 (68.0%)	< 0.001	3.63	1.526-8.654	0.004
Luminal diameter ( $\leq$ 3.35 mm vs > 3.35 mm)	35 (28.5%)	71 (94.7%)	< 0.001	20.92	6.701-65.293	< 0.001
Upstream lumen ( $\geq$ 27.5 mm vs < 27.5 mm)	35 (28.5%)	63 (84.0%)	< 0.001	4.57	1.61-12.982	0.004
Fibrostenosis score (mild to moderate vs severe)	78 (63.4%)	15 (20.0%)	< 0.001	0.89	0.305-2.595	0.83
Combined variable X ( $\leq -2.9566 \text{ vs} > -2.9566$ )	25 (20.3%)	70 (93.3%)	< 0.001			

CTE computed tomography enterography, CD Crohn's disease, OR odds ratio, CI confidence interval

of > -2.9566 highly predicted the success of medical therapy for symptomatic stricturing CD.

A nomogram was developed by translating the multiple logistic regression. The bowel wall thickness, luminal stenosis, and upstream lumen were selected for constructing the nomogram (Fig. 2). We excluded the combined CTE variable from the model since the interaction effect of the variable. A total score could be easily calculated to estimate **Fig. 1** Diagnostic value of CTE variables for predicting surgical-free survival and the calculation of combined CTE variable

Variables	Cutoff value	Sensitivity	Specificity	Area under curve (95% confidence interval )	P value
Wall thickness	5.90	0.81	0.68	0.80 (0.73-0.87)	< 0.001
Upstream lumen	27.50	0.72	0.84	0.82 (0.75-0.87)	< 0.001
Luminal diameter	3.35	0.95	0.72	0.87 (0.82-0.92)	< 0.001
Combined CTE variable	-2.96	0.93	0.80	0.91 (0.85-0.95)	< 0.001



Calculation of ccombined CTE variable based on the logistic regression of CTE variables for surgical-free survival.

Variables	Odds ratio	P value	95% confidence interval
Wall thickness	-0.248	0.02	0.63-0.96
Upstream lumen	-0.112	< 0.01	0.84-0.95
Luminal diameter	0.730	< 0.01	1.48-2.91

Combined CTE variable=  $[0.73 \times Luminal diameter - 0.112 \times Upstream]$ 

**Fig. 2** A nomogram predicting surgical-free survival in symptomatic stricturing Crohn's disease patients. Factors must be vertically referred to the point line and the sum of points is then calculated for a single patient



lumen - 0.248 × Wall thickness]/0.73

the probability of surgical-free survival by projecting the total score on the total point scale.

The C-indexes of the nomogram in the primary and validation cohorts were 0.905 (95% CI 0.860–0.950) and 0.892 (95% CI 0.784–0.982), indicating relatively good discrimination of this model. The calibration plots of the nomogram for the probability of surgical-free survival in the primary and validation cohorts are presented in Fig. 3. A good concordance was observed between the predicted and actual probabilities.

## **Decision curve analysis**

Decision curve analysis was used to evaluate the utility of the predictive model for clinical decision-making. As seen in Fig. 4, horizontal black line meant NB when all patients received surgery and left gray line meant NB when all patients were treated with non-surgical intervention. The logistic predictive model (red line) provided a larger NB across the range of threshold probability compared with that of the other three CTE parameters alone.

## Histopathological findings and the correlation between CTE parameters and pathological characteristics

We compared the pathological differences between the stenotic loops and resection margins in 15 CD patients. As a result, muscular hyperplasia/hypertrophy and chronic inflammation throughout all layers were the first and second most significant changes in stenotic bowel compared with resection margins (Table\_3\_SuppInfo). The scores of bowel wall chronic inflammation and muscular hyperplasia/hypertrophy were significantly higher in patients with combined CTE variable under -2.5966 than that of the opposite ones (Table\_4\_SuppInfo). The score of bowel

**Fig. 3** C-indexes [0.905 in primary cohort (**a**) and 0.892 in validation cohort (**c**)] and calibration plots [in the primary cohort (**b**) and the validation cohort (**d**)] for checking the concordance between the nomogram-predicted and actual probability of surgical-free survival in primary and validation cohorts



**Fig. 4** Decision curve analysis. Horizontal black line meant the net benefit (NB) when all patients received surgery and left gray line meant NB when all patients were treated medically. The logistic predicting model (red line) provided a larger NB across the range of threshold probability compared with the individual computed tomography enterography parameters

wall muscular hyperplasia/hypertrophy was significantly correlated to the diameter of luminal stenosis (Spearman's r = -0.655, p = 0.008) and combined CTE variable (Spearman's r = 0.683, p = 0.005).

# Discussion

Our study has identified specific CTE features that are highly predictive of surgical-free survival in symptomatic stricturing CD patients, providing an alternative strategy to surgery and adding to our understanding of the natural history of the complication. In the present study, surgical-free survival significantly correlated with main CTE features (bowel wall thickness < 5.9 mm, luminal diameter > 3.35 mm, upstream lumen < 27.5 mm or combined CTE variable > -2.9566) but not inflammatory characters (mucosal enhancement, mural stratification, comb sign, etc.). These results verified the notion that surgical-free survival in symptomatic stricturing CD was determined by the absence of fibrotic component rather than the co-existing inflammatory lesion of the narrow bowel [6]. In the multiple logistic regression, wall thickness, luminal stenosis, and upstream lumen could predict surgical-free survival in these CD patients independently. The nomogram of the three independent CTE variables performed well in predicting the probability of surgical-free survival in symptomatic stricturing CD patients. And its predictive ability was supported by the C-indexes value and the calibration curves in primary and validation cohorts. Furthermore, from the decision curve analysis, the predictive model provided greater clinical usefulness compared with that of the single CTE parameter, thus assisting clinical decision-making of whether a symptomatic stricture could benefit from non-surgical intervention. Additionally, the CTE parameters including luminal stenosis and combined CTE variable might correlate well with the predominant histopathological changes of stenotic bowel (muscular hyperplasia/hypertrophy and chronic inflammation), at some extent, strengthening the confidence of non-surgical intervention for CD-associated strictures.

Several previous studies had investigated the medical response or surgical risks of stricturing CD [4, 8, 19, 20]. As a result, 31–54% stricturing CD patients underwent surgical-free survival during 41–60 months follow-up. The observed factors associated with medical response were biologics treatment, the absence of penetrating disease, and bowel resection history. The surgical risks were the presence of upstream lumen (over 25–30 mm), severe obstructive symptoms (CD obstructive score over 4), and longer stricture(s) length (over 5–12 cm). To date, CD-associated strictures were not clearly defined [6, 21]. The CREOLE study with 97 CD patients defined stricture as "occurrence of constant luminal narrowing with

prestenotic dilatation or obstructive signs/symptoms" [8, 19]. The BACARDI study identified ileal stricturing CD as "at least 50% of luminal narrowing in the presence of radiological signs" [4]. Another research regarded CD strictures as  $\geq 80\%$  luminal reduction compared to proximal bowel, bowel wall thickness > 3 mm, and narrowing present on all magnetic resonance enterography acquisitions [20]. However, it was worth noting that obstructive symptoms were not compulsory in these conclusion criteria. Additionally, bowel resection history and the concomitant fistula were associated with higher surgical risk in CD-associated strictures according to the previous results [4, 8, 19, 20]. Therefore, we included purely stricturing CD patients suffering from obstructive symptom(s) with strictures confirmed by radiologists. Those with surgical history, fistula/abscess, and no clinical symptom(s) were excluded from our cohorts, thus making our study to target the clinical course of the subtype of CD patients.

Although surgical intervention should be preferred for fibrotic strictures, anti-inflammatory therapy may maintain clinical remission without surgical intervention for several years in selected stricturing CD [22]. Theoretically, the strictures might be predominantly inflammatory at the early stage of disease and then gradually became fibrotic. And medical treatment is effective for inflammatory lesions but not fibrotic stenosis [23]. Previous researches had explored the correlation between cross-sectional imaging characteristics and histological features of CD-associated strictures and reported inconsistent results [12, 24]. Therefore, differentiating fibrosis from inflammation by current cross-sectional imaging techniques still remained challenging [7, 11, 12]. The reason might be that these cross-sectional imaging techniques were based on the unconfirmed pathological scoring systems for assessment of fibromuscular stenosis, leading to the substantial heterogeneity among different researches [13]. Consequently, we adopted the CD stenosis scoring system from Chen et al [14] accounting for degrees of several histopathologic changes specific to each mural layer separately, which was considered as the best one among the various pathological scoring methods [25]. In accordance with their results, our data suggested that the muscular hyperplasia/hypertrophy throughout the whole layers was the most significant change between stenotic bowel and resection margin [14]. While the volume expansion was most significantly expanded in submucosa than other layers which differed from the previous study [14]. The reasons might rely on the different races, pathogenesis, and disease duration of analyzed samples. And the combined CTE variable was significantly correlated with the most significant pathological change of fibromuscular stricture (hypertrophy/hyperplasia), thus adding pathologic evidence of CTE predicting surgicalfree survival in symptomatic stricturing CD patients.

Some limitations existed. Firstly, this was a retrospective research from a single institution. Therefore, recall and selection biases were inevitable. Secondly, we did not include clinical items, since we aimed to investigate the predictive value of the objective CTE features for surgical-free survival in obstructive stricturing CD patients. Thirdly, the relationship between CTE variables and histological scores in non-surgical group could not be evaluated. Fourthly, the phenomenon that anti-TNFs could improve nature course of CD was not observed in the present study, which might be associated with the fewer patients treated with biologics in our cohorts.

# Conclusions

In patients with symptomatic stricturing CD, CTE parameters including wall thickness < 5.9 mm, luminal stenosis > 3.35 mm, upstream lumen < 27.5 mm, and the combined CTE variable > -2.9566 are highly predictive of disease course and surgical-free survival, suggesting the important role of CTE in decision-making of treatment options. Further prospective studies are warranted to confirm these results.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00261-022-03588-0.

Funding This study was supported by National Natural Science Foundation of China (Grant 82170573, 81770556, and 81670471).

#### **Declarations of interest**

**Conflict of interest** The authors declare that they have no competing interest.

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