Prognostic Significance of The Diameter of Superior Rectal Vein For Locally Advanced Rectal Cancer

Yafang Hong

Fujian Medical University Union Hospital

Runfan Chen

Fujian Medical University Union Hospital

Anchuan Li

Fujian Medical University Union Hospital

Benhua Xu (✉ benhuaxu@sina.com)

Fujian Medical University Union Hospital <https://orcid.org/0000-0002-9279-1254>

Research Article

Keywords: superior rectal vein, locally advanced rectal cancer, metastasis-free survival, overall survival

Posted Date: January 18th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1264895/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Objectives: The purpose of this study was to evaluate the association between the diameter of the superior rectal vein (dSRV) and prognosis in patients with locally advanced rectal cancer (LARC).

Methods and materials: This retrospective study included 420 patients with LARC who received neoadjuvant therapy followed by total mesorectal resection (TME) from December 2014 to July 2017. The dSRV was measured before treatment. The maximal χ^2 method was employed to determine the dSRV threshold of 3.6 mm based on the difference in disease-free survival, and then to divide the patients into 2 groups. The propensity score matching method (PSM) was used to balance the individual characteristics between the two groups. Kaplan–Meier curves and adjusted Cox models were used to determine the relationship among the baseline characteristics and overall survival (OS), disease-free survival (DFS), metastasis-free survival (MFS) and local recurrence-free survival (LRFS).

Results: During a median follow-up of 45 months, 7 patients had relapse (1.60%), and 71 had distant metastasis (16.90%). Kaplan–Meier survival curves showed that patients with a dSRV > 3.60 mm had better survival (dSRV > 3.60 mm vs. $\leq$ 3.60 mm: 3-y MFS: 87.70% vs. 68.20%, $P < 0.001$; 3-y DFS: 85.50% vs. 64.20%, $p < 0.001$; 3-y OS: 91.90% vs. 82.20%, $p=0.005$). The multivariate Cox regression analysis after adjusting the covariates and the multivariate Cox regression analysis after performing PSM showed that the dSRV was an independent prognostic factor for MFS, DFS and OS.

Conclusion: The dSRV measurement is valuable in predicting the prognosis of patients with LARC, and the prognosis of patients with a smaller dSRV seems to be poor.

Introduction

With lifestyle changes, the prevalence of colorectal cancer increases, which is a serious threat to human life around the world. According to the Global Cancer Epidemiology Statistics (GLOBOCAN 2021) released by the International Cancer Organization Research Institute of WHO in 2021, the incidence of colorectal cancer is 10% and ranked third among different types of cancers in 2020, and the death rate ranked second at 9.4%.⁽¹⁾ However, due to the widespread use of neoadjuvant chemoradiotherapy followed by TME surgery, the local recurrence of LARC has decreased significantly, and the 10-year local recurrence rate has been controlled at 5%-7.1%. The main pattern of treatment failure is distant metastasis, and the cumulative 10-year incidence rate is approximately 25%- 29.8%,^(2, 3) which is an important factor affecting the survival of patients with LARC. Therefore, early identification of patients at high risk of metastasis and the use of intensive systemic treatment may improve patient survival.

When the tissue or organ undergoes pathological changes, its blood reflux and the diameter of its draining vein will change.⁽⁴⁾ The superior rectal vein collects the left and right branch veins from the rectal venous plexus and continues as the inferior mesenteric vein. The SRV collects venous blood from the upper 2/3 segment of the rectum and is the main draining vein of the rectum. It has been reported that the inferior mesenteric vein of patients with rectal cancer is wider than that of patients without

cancer (5.9 mm vs. 4.7 mm, $p < 0.001$),(5) and the diameter of the superior rectal vein of patients with rectal cancer with distant metastasis is wider than that of patients with nonmetastatic cancer (4.0 mm vs. 3.3 mm, $p=0.044$).(6)

Some studies have found that the dSRV can not only be used as a predictor of lymphatic vascular invasion and lymph node metastasis of rectal cancer (6, 7) but is also valuable in determining whether liver lesions are metastatic lesions and predicting KRAS mutations in rectal cancer. (8, 9) Although it has been reported that the dSRV in patients with metastasis is wider than that in patients without metastasis, (6) some studies have reported different results, and there is no significant difference in the dSRV between patients with metastasis and those without metastasis.(7) At present, research on the role of the superior rectal vein in rectal cancer is still controversial, and the related studies are few. The existing studies are small sample analyses, and there may be bias. Therefore, this study intends to expand the sample size to explore the correlation between the dSRV and the prognosis of patients with LARC after neoadjuvant therapy to provide more evidence for the evaluation and prognosis of patients with LARC.

Methods

Patients

We reviewed patients with LARC who received neoadjuvant therapy followed by TME surgery in our unit from December 2014 to July 2017. The research design was conducted in accordance with the ethical guidelines for human research and was approved by the institutional review committee or the ethics committee. Patients with rectal cancer confirmed by histopathology were included in this study. Patients with complete imaging data, such as chest CT, abdominal and pelvic MRI, transrectal ultrasound and postoperative pathological data, were included in this study.

Patients with the following conditions at the time of diagnosis were excluded: multiple tumors of the digestive system, intra-abdominal vein thrombosis or stenosis, pelvic congestion syndrome, portal hypertension or ascites, local tumor resection, previous tumor-related treatment (chemotherapy or pelvic radiotherapy) and unclear superior rectal veins.

Measurement of the dSRV

The dSRV was measured on simulated CT images. All patients were advised to fast for 8 hours before the CT scan. The bladder was emptied one hour before the scan, 500 ml drinking water was consumed half an hour before scanning (10 ml 76% compound meglumine diatrizoate was added to the water for the development of the small intestine), and urine was held back. In the supine position, the patients' abdomen and pelvis were fixed with polymer memory omentum. Approximately 90 mL contrast medium (iopramine injection) was injected through the median cubital vein at a rate of 3 ml/s. The GE Lightspeed large aperture CT simulator was used. The scanning range was from the lower edge of the second lumbar vertebra to the middle section of the femur. The scanning distance and thickness were 0.5 cm. The

simulated CT images were transmitted to the treatment planning system (Eclipse13.5 version) through the local area network for image postprocessing.

The dSRV was measured by 2 physicians under the guidance of a senior professional title imaging physician. We chose the second sacral vertebrae as the measured level. At this level, the vessels were horizontal in most cases, and the filling of surrounding adipose tissue made them easy to identify (Figure 1). The superior rectal vein has pairs of branch veins and continues as the inferior mesenteric vein. We identified the superior rectal vein by identifying its reflux path on a series of adjacent axial CT images. The superior rectal veins can be identified by recognizing their paired tributaries, as well as their own reflux paths. After viewing the image 4 times, a clear and uniform section of the SRV was measured to determine the diameter.(5) The average value of the readings of two physicians was taken as the final diameter of the superior rectal vein.

Therapy

All patients received neoadjuvant chemoradiotherapy and subsequently underwent TME surgery. The preoperative radiotherapy consisted of 50.4Gy radiation in 25 fractions over 5 weeks, with intensity-modulated radiotherapy using 6-MV x-rays, delivered to the primary tumor and the mesentery of rectum, presacral region, pelvic sidewall, the two end portions of rectum and the pelvis internal iliac lymph drainage areas. The synchronous chemotherapy regimens included the Xelox, capecitabine and Folfox4 regimens. Surgery was performed 6-8 weeks after chemoradiotherapy, and the operation was performed in strict accordance with the principle of TME operation.

Follow up

Number of patient deaths, tumor recurrence and metastasis were collected. Overall survival (OS) was defined as the interval between the first day of treatment and the occurrence of death or the last follow-up (whichever first occurred). Disease-free survival (DFS) was defined as the interval between the first day after operation and the occurrence of recurrence, metastasis or death (for any reason). Local recurrence-free survival (LRFS) was defined as the interval from the first day after operation to local regional recurrence, death or final follow-up. Distant metastasis-free survival (DMFS) was defined as the date from the first day of treatment to distant metastasis, death or final follow-up.

Patients were followed up by outpatient services and telephone. They were required to review at regular intervals of 3 months for two years after surgery and then every 6 months for the next 3 years. Physical examination, chest CT, enhanced MRI scan of the abdomen and pelvis, serum carcinoembryonic antigen and carbohydrate antigen 19-9 were proposed at each visit. Colonoscopy was recommended 3 months after the operation and once a year thereafter. Follow-up period ended on February 1, 2020.

Statistical analysis

X-tile software was used to calculate the optimal threshold value of the dSRV according to the difference in survival curves. Patients were divided into two groups according to the value. The difference in

baseline characteristics between the two groups was compared by chi-square or Fisher's exact tests. Selection bias was inevitable because this study was a retrospective observational study. The propensity score matching (PSM) method was used to minimize the risk of bias. The patients were matched at a 1:1 ratio using a combination of nearest neighbor methods, and the caliper value was set to 0.05. The Kaplan–Meier method was adopted to estimate OS, DFS, MFS and LRFS. Factors affecting survival were analyzed by multivariate Cox proportional hazard regression. A $P < 0.05$ was considered statistically significant, and all statistical analyses were performed using the Social Sciences (SPSS) version 25.0 for Windows.

Results

Deciding the cutoff value and grouping

We used X-tile software to determine the threshold value of pretreatment dSRV associated with 3-year DFS in patients with LARC. The optimum cutoff value we obtained was 3.60 mm. The patients were divided into two groups according to $\text{dSRV} > 3.60 \text{ mm}$ or $\leq 3.60 \text{ mm}$.

Patients' characteristics and PSM

The detailed parameters of the clinicopathological characteristics are summarized in Table 1. A total of 420 patients with LARC were enrolled in our study: 273 were male and 147 were female. The proportion of male patients was higher in the $\text{dSRV} > 3.60 \text{ mm}$ group (70.9% vs. 42.5%, $p < 0.001$). Elderly patients who had a tumor length less than 5 cm and a distance to the anus greater than 7 cm were concentrated in the $\text{dSRV} \leq 3.60 \text{ mm}$ group, with a significant difference between the two groups. Considering that previous studies have found that EMVI has an effect on dSRV,(10) these factors are taken as covariates of propensity score matching. Finally, 82 pairs were successfully matched. After matching, the baselines of the two groups were balanced. The results are detailed in Table 1.

Table 1
Comparison of Patient Characteristics According to dSRV

Characteristics	Overall Dataset		p	Propensity Score-matched Group		p
	≤3.60 mm	>3.60 mm		≤3.60 mm	>3.60 mm	
	(N=87),n(%)	(N=333),n(%)		(N=82),n(%)	(N=82),n(%)	
Age			0.046			0.592
≤65 years	59(67.8)	262(78.7)		59(72.0)	63(76.8)	
>65 years	28(32.2)	71(21.3)		23(28.0)	19(23.2)	
Sex			0.000			0.753
Male	37(42.5)	236(70.9)		37(45.1)	34(41.5)	
Female	50(57.5)	97(29.1)		45(54.9)	48(58.5)	
Distance to anus(cm)			0.034			0.840
≤7 cm	74(85.1)	246(73.9)		69(84.1)	67(81.7)	
>7 cm	13(14.9)	87(26.1)		13(15.9)	15(18.3)	
Tumor length			0.001			0.161
≤5 cm	67(77.0)	193(58.0)		64(78.0)	55(67.1)	
>5 cm	20(23.0)	140(42.0)		18(22.0)	27(32.9)	
EMVI			0.718			0.875
+	38(43.7)	154(46.2)		36(43.9)	38(46.3)	
-	49(56.3)	179(53.8)		46(56.1)	44(53.7)	
Clinical TNM stage			0.332			0.167
I	8(9.2)	20(6.0)		7(8.5)	2(2.4)	
II	79(90.8)	313(94.0)		75(91.5)	80(97.6)	
Pathological tumor response			0.443			0.982
TRG 0	21(24.1)	78(23.4)		20(24.4)	18(22.0)	
TRG 1	32(36.8)	98(29.4)		29(35.4)	29(35.4)	
TRG 2	28(32.2)	137(41.1)		28(34.1)	30(36.6)	

EMVI, extramural venous invasion; TRG, tumor regression grade; pCR, pathological complete response.

Characteristics	Overall Dataset		p	Propensity Score-matched Group		p
	≤ 3.60 mm	> 3.60 mm		≤ 3.60 mm	> 3.60 mm	
	(N=87),n(%)	(N=333),n(%)		(N=82),n(%)	(N=82),n(%)	
TRG 3	6(6.9)	20(6.0)		5(6.1)	5(6.1)	
ypT			0.287			-
0	21(24.1)	79(23.7)		20(24.4)	19(23.2)	
1	3(3.4)	18(5.4)		2(2.4)	7(8.5)	
2	32(36.8)	85(25.5)		31(37.8)	21(25.6)	
3	29(33.3)	142(42.6)		27(32.9)	32(39.0)	
4	2(2.3)	9(2.7)		2(2.4)	3(3.7)	
ypN(0/1-2)			0.890			0.195
0	64(73.6)	249(74.8)		59(72.0)	67(81.7)	
1-2	23(26.4)	84(25.2)		23(28.0)	15(18.3)	
Pathological TNM stage			0.653			0.354
pCR	20(23.0)	76(22.8)		19(23.2)	17(20.7)	
+	25(28.7)	82(24.6)		23(28.0)	23(28.0)	
-	18(20.7)	90(27.0)		17(20.7)	26(31.7)	
-	24(27.6)	85(25.5)		23(28.0)	16(19.5)	
EMVI, extramural venous invasion; TRG, tumor regression grade; pCR, pathological complete response.						

Survival Analysis

The median follow-up period for all patients was 45 months (7-61 months). During the follow-up, 7 patients had disease recurrence (1.60%), and 71 patients had distant metastasis (16.90%).

As shown in Figure 2, the survival curves of the two groups differed significantly. The 3-year MFS, 3-year DFS, and 3-year OS rates were 87.70%, 85.50% and 91.90% in the dSRV >3.60 mm group and 68.20% ($p<0.001$) and 64.20% ($p<0.001$) and 82.20% ($p=0.005$) in the other group, respectively. In the Cox hazard model, univariate and multivariate analyses were employed to evaluate the significance of the dSRV as an independent prognostic factor. As shown in Table 2, within our groups, dSRV, EMVI ypT stage, ypN stage and TRG were associated with OS, DFS and MFS. In the multivariate analysis, dSRV ≤ 3.60 mm was

significantly correlated with poor OS (HR=2.16, 95% CI: 1.22–3.84, p=0.009), DFS (HR=2.80, 95% CI: 1.80–4.36, p<0.001) and MFS (HR=2.95, 95% CI: 1.83–4.76, p<0.001). After propensity score matching, the dSRV>3.60 mm group maintained an advantage in OS, DFS and MFS. The results are detailed in Table 2.

Table 2
Significant Factors in Survival Analysis

Variables	Univariate Analysis ^a	Multivariate Analysis ^a		Univariate Analysis ^b	Multivariate Analysis ^b	
	p	p	HR (95% CI)	p	p	HR (95% CI)
OS						
dSRV	0.007	0.009	2.16(1.22-3.84)	0.033	0.033	1.61(1.04-2.49)
EMVI	0.001	0.003	2.48(1.36-4.50)	0.007	0.008	3.29(1.37-7.88)
ypT	0.005	0.513	1.15(0.76-1.72)	NS	NS	NS
ypN	0.005	0.002	2.41(1.38-4.20)	0.015	NS	NS
TRG	0.013	0.475	1.20(0.73-1.20)	NS	NS	NS
DFS						
dSRV	0.000	0.000	2.80(1.80-4.36)	0.004	0.013	1.52(1.09-2.10)
EMVI	0.003	0.030	1.65(1.05-2.59)	0.015	0.052	1.85(1.00-3.44)
ypT	0.001	0.063	1.23(0.99-1.53)	NS	NS	NS
ypN	0.000	0.001	2.15(1.36-3.39)	0.000	0.007	2.33(1.26-4.33)
TRG	0.004	0.641	1.10(0.75-1.61)	NS	NS	NS
MFS						
dSRV	0.000	0.000	2.95(1.83-4.76)	0.017	0.046	1.41(1.01-1.97)
EMVI	0.007	0.057	1.61(0.99-2.63)	0.014	0.050	1.92(1.00-3.70)
ypT	0.001	0.046	1.28(1.00-1.63)	NS	NS	NS
a: survival analysis for overall dataset						
b: survival analysis for Propensity Score-matched Group						
NS Not significant						

Variables	Univariate Analysis ^a	Multivariate Analysis ^a		Univariate Analysis ^b	Multivariate Analysis ^b	
	p	p	HR (95% CI)	p	p	HR (95% CI)
ypN	0.000	0.004	2.07(1.26-3.39)	0.000	0.004	2.58(1.36-4.92)
TRG	0.013	0.964	0.99(0.65-1.51)	NS	NS	NS
LRFS						
ypN	0.013	0.013	8.02(1.56-41.37)	0.010	0.039	10.89(1.13-104.85)
a: survival analysis for overall dataset						
b: survival analysis for Propensity Score-matched Group						
NS Not significant						

Discussion

Through neoadjuvant chemoradiotherapy followed by optimized total mesorectal excision, the local recurrence rate of locally advanced rectal cancer was significantly reduced to less than 5%.(3, 11, 12) Distant metastasis has become the main pattern of treatment failure for rectal cancer. The study reported that approximately 15% - 24.4% of patients had metastasis within 5 years after the operation. (13, 14) In this study, the 4-year cumulative local recurrence rate was 1.60%, and approximately 16.90% of patients had distant metastasis, which was basically consistent with previous studies. Better control of systemic diseases has become the major challenge in the treatment of LARC.

We found that the diameter of the superior rectal vein was an independent prognostic factor for OS, DFS and MFS. Patients whose superior rectal vein diameter was greater than 3.60 mm showed better survival outcomes than those with a small diameter. Bakke et al. discovered that the low tumor blood flow (BF) shown by dynamic enhanced MRI was an adverse prognostic indicator of progress-free survival and overall survival and indicated that the tumor had a poor response to neoadjuvant therapy.(15) Proximal venous obstruction and increased distal blood flow are the two main mechanisms of venous dilatation. Therefore, patients with rectal cancer and poor prognosis have less tumor blood flow and a smaller diameter of the superior rectal vein.

Metastasis is the most important cause affecting the survival of patients with tumors. Hypoxia and nutrient deficiency in the tumor microenvironment affect the occurrence of tumor metastasis.(16) The rapid proliferation of tumor cells requires oxygen support, but the quality of new tumor blood vessels is poor, so the structure of the blood vessel wall is incomplete, the blood vessel network is disordered, and the diffusion distance of oxygen is less than the distance between capillaries, causes hypoxia.(17) The

risk of metastasis and death increases as tumor hypoxia increases. (18-20) Tumors with poor blood perfusion has less oxygen and nutrients, and the tumor has more severe hypoxia, thus mobilizing the tumor cells to leave the primary site to find a more suitable survival site. (15) Tumors with poor prognosis have less blood flow, causing less blood reflux. Hence, there was no significant change in the drainage vein, and the diameter of the reflux vein was small.

Wu et al. investigated whether the dSRV in patients with distant metastasis was larger than that in patients without rectal cancer,(6) while Li Xinwen et al. reported that there was no significant difference in the dSRV between patients with metastasis and patients without metastasis.(7) Interestingly, our study showed conflicting results. Patients with a dSRV less than 3.60 mm had a greater risk of distant metastasis during follow-up. The reason for this result may be related to the study population. The metastasis of patients in previous studies already existed when they were included in the analysis, while the population selected in our study was patients with stage II-III rectal cancer, and distant metastasis occurred during postoperative follow-up.

EMVI has been identified as a poor prognostic factor independent of the staging system for rectal cancer. (21-23) Several studies have shown that changes in the diameter of the superior rectal vein and inferior mesenteric vein (IMV) may be CT manifestations of EMVI. The superior rectal vein and inferior mesenteric vein are the main drainage veins of the rectum. Venous thrombosis and increased venous drainage may affect the diameter of the SRV and IMV in patients with rectal cancer with positive EMVI. (6) It has been found that when dSRV is restricted to 3.95 mm, EMVI can be properly diagnosed with high accuracy, sensitivity (93.30%) and specificity (67.90%), and the area under the curve was 0.85 ± 0.05 ($p < 0.001$). (10)

At present, EMVI diagnosis mainly depends on MRI, but due to the limited resolution of MRI images, if there are tumors in perirectal lymphatic vessels, the evaluation of EMVI on MRI may lead to false-positives. In addition, on T2-weighted imaging, tumor subserosal invasion without perirectal vein invasion, connective tissue hyperplasia or disappearance of the perirectal vein signal cavity were other potential sources of false-positive MRI results.(24, 25) Therefore, on the basis of the current diagnosis, increasing the index of superior rectal vein diameter may increase the accuracy of EMVI diagnosis.

The response to neoadjuvant therapy can be predicted by measuring and comparing the diameter changes of SRV and IMV pre- and post-neoadjuvant therapy. (5, 26) Ivan et al. proposed that the IMV diameter may be used to evaluate the response to neoadjuvant chemoradiotherapy for locally advanced rectal cancer and may be a potential surrogate marker. Compared with non-responders, the mean IMV diameter of responders decreased by 17.54%, and that of non-responders increased by 1.39%, $p = 0.0001$. (5) Due to the lack of abdominal and pelvic CT data after neoadjuvant therapy, the changes in superior rectal vein diameter pre- and post-neoadjuvant therapy were not compared.

There are still some deficiencies in our study. First, as a retrospective study, only the patients treated in this unit may have a certain degree of selective bias and retrospective bias. Second, because of the

submillimeter differences in the SRV measurements and existing vascular variation, there may be measurement errors in the superior rectal vein diameter. While it has been distinctly required to determine the measurement at the time of research and design, the average value is taken after independent measurement by two physicians to minimize measurement error. Therefore, before it is applied to daily practice, more large-scale multicenter studies and staged samples are needed for further research.

Conclusion

The hemodynamic changes in rectal cancer lesions may be reflected by measuring the diameter of the superior rectal vein, which is a potential prognostic indicator of concern.

Abbreviations

dSRV, diameter of superior rectal vein

LARC, locally advanced rectal cancer

TME, total mesorectal resection

PSM, propensity score matching

OS, overall survival

DFS, disease-free survival

MFS, metastasis-free survival

LRFS, local recurrence-free survival

EMVI, extramural venous invasion

TRG, tumor regression grade

pCR, pathological complete response

BF, blood flow

IMV, inferior mesenteric vein

Declarations

Ethics approval and consent to participate

Although patient consent was not specifically obtained for this analysis, all information was retrospectively extracted in the context of compliance with the ethical standards of the institutional

and/or national research committees and with the principles of the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Patient medical records were analyzed retrospectively, with no individual patient identifiable information used. Thus, the Fujian Medical University Union Hospital Ethics Review Board deemed patient consent unnecessary.

Acknowledgements

The authors thank the volunteers for their participation in these studies.

Authors' contributions

YH: Data collection, statistics, original draft. RC: Data collection. AL, BX: Conception and design, review and editing the manuscript. All authors read and approved the final manuscript.

Funding

This work was supported by the Fujian provincial health technology project [grant number 2021CXA011] and the Joint Funds for the innocation of science and Technology, Fujian province [grant number 2017Y9061].

Availability of supporting data The data used to support the findings of this study are available from the corresponding author upon request.

Consent for publication

The manuscript has been approved by all authors for publication.

Competing interests

All authors have no conflicts of interest to declare.

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics. 2021. CA: a cancer journal for clinicians. 2021;71(1):7-33.
2. van Gijn W, Marijnen CA, Nagtegaal ID, Kranenbarg EM, Putter H, Wiggers T, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. The Lancet Oncology. 2011;12(6):575–82.
3. Sauer R, Becker H, Hohenberger W, Rodel C, Wittekind C, Fietkau R, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med. 2004;351(17):1731–40.
4. Feng ST, Chan T, Sun CH, Li ZP, Guo HY, Yang GQ, et al. Multiphasic MDCT in small bowel volvulus. Eur J Radiol. 2010;76(2):e13-8.

5. Ivan CV, Mullineux JH, Verma R, Shah V, De A, Elabassy M, et al. Assessment of the inferior mesenteric vein diameter as a surrogate marker to evaluate response to neoadjuvant chemoradiotherapy for locally advanced rectal adenocarcinoma. *Colorectal disease: the official journal of the Association of Coloproctology of Great Britain Ireland*. 2017;19(12):1076–80.
6. Wu CC, Lee RC, Chang CY. Prediction of lymphovascular invasion in rectal cancer by preoperative CT. *Am J Roentgenol*. 2013;201(5):985–92.
7. Li X, Song C, Cai H, Jia Y, Peng Z, Li Z, et al. Correlation between the Diameter of Superior Rectal Vein and Inferior Mesenteric Vein and the Lymph Node Metastasis of Rectal Carcinoma. *sunyat-senuniv(medsci)*. 2017;38:538–44.
8. Kang KA, Jang KM, Kim SH, Kang TW, Cha DI. Risk factor assessment to predict the likelihood of a diagnosis of metastasis for indeterminate hepatic lesions found at computed tomography in patients with rectal cancer. *Clin Radiol*. 2017;72(6):473–81.
9. Song C, Shen B, Dong Z, Fan Z, Xu L, Li ZP, et al. Diameter of Superior Rectal Vein - CT Predictor of KRAS Mutation in Rectal Carcinoma. *Cancer management research*. 2020;12:10919–28.
10. Gursoy Coruh A, Peker E, Elhan A, Erden I, Erden A. Evaluation of Extramural Venous Invasion by Diffusion-Weighted Magnetic Resonance Imaging and Computed Tomography in Rectal Adenocarcinoma. *Can Assoc Radiol J*. 2019;70(4):457–65.
11. Gerard JP, Conroy T, Bonnetain F, Bouche O, Chapet O, Closon-Dejardin MT, et al. Preoperative radiotherapy with or without concurrent fluorouracil and leucovorin in T3-4 rectal cancers: results of FFCD 9203. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*. 2006;24(28):4620–5.
12. Rodel C, Graeven U, Fietkau R, Hohenberger W, Hothorn T, Arnold D, et al. Oxaliplatin added to fluorouracil-based preoperative chemoradiotherapy and postoperative chemotherapy of locally advanced rectal cancer (the German CAO/ARO/AIO-04 study): final results of the multicentre, open-label, randomised, phase 3 trial. *The Lancet Oncology*. 2015;16(8):979–89.
13. Wang F, Fan W, Peng J, Lu Z, Pan Z, Li L, et al. Total mesorectal excision with or without preoperative chemoradiotherapy for resectable mid/low rectal cancer: a long-term analysis of a prospective, single-center, randomized trial. *Cancer communications (London England)*. 2018;38(1):73.
14. Tang J, Wu X, Bai Y, Gao Y, Jiang W, Kong L, et al. Long-Term Outcome of Oxaliplatin and Capecitabine (XELOX) Concomitant with Neoadjuvant Radiotherapy and Extended to the Resting Period in High Risk Locally Advanced Rectal Cancer. *J Cancer*. 2018;9(8):1365–70.
15. Bakke KM, Meltzer S, Grøvik E, Negård A, Holmedal SH, Gjesdal KI, et al. Sex differences and tumor blood flow from dynamic susceptibility contrast MRI are associated with treatment response after chemoradiation and long-term survival in rectal cancer. *Radiology*. 2020;297(2):352–60.
16. Polachek WJ, Zervantonakis IK, Kamm RD. Tumor cell migration in complex microenvironments. *Cell Mol Life Sci*. 2013;70(8):1335–56.
17. Sorg BS, Hardee ME, Agarwal N, Moeller BJ, Dewhirst MW. Spectral imaging facilitates visualization and measurements of unstable and abnormal microvascular oxygen transport in tumors. *Journal of*

- biomedical optics. 2008;13(1):014026.
18. Vaupel P, Mayer A, Hockel M. Tumor hypoxia and malignant progression. *Methods Enzymol.* 2004;381:335–54.
 19. Vaupel P. Prognostic potential of the pre-therapeutic tumor oxygenation status. *Adv Exp Med Biol.* 2009;645:241–6.
 20. Vaupel P, Hockel M, Mayer A. Detection and characterization of tumor hypoxia using pO₂ histography. *Antioxid Redox Signal.* 2007;9(8):1221–35.
 21. Yao X, Yang SX, Song XH, Cui YC, Ye YJ, Wang Y. Prognostic significance of computed tomography-detected extramural vascular invasion in colon cancer. *World journal of gastroenterology.* 2016;22(31):7157–65.
 22. Dighe S, Swift I, Magill L, Handley K, Gray R, Quirke P, et al. Accuracy of radiological staging in identifying high-risk colon cancer patients suitable for neoadjuvant chemotherapy: a multicentre experience. *Colorectal disease: the official journal of the Association of Coloproctology of Great Britain Ireland.* 2012;14(4):438–44.
 23. Chand M, Swift RI, Tekkis PP, Chau I, Brown G. Extramural venous invasion is a potential imaging predictive biomarker of neoadjuvant treatment in rectal cancer. *British journal of cancer.* 2014;110(1):19–25.
 24. Ahn JH, Kim SH, Son JH, Jo SJ. Added value of diffusion-weighted imaging for evaluation of extramural venous invasion in patients with primary rectal cancer. *Br J Radiol.* 2019;92(1096):20180821.
 25. Bae JS, Kim SH, Hur BY, Chang W, Park J, Park HE, et al. Prognostic value of MRI in assessing extramural venous invasion in rectal cancer: multi-readers' diagnostic performance. *European radiology.* 2019;29(8):4379–88.
 26. Zhu H, Wei Z, Huang W, Chen Z. Application value of diameter change of superior rectal vein and inferior mesenteric vein by CT examination in the efficacy evaluation of neoadjuvant therapy for locally advanced rectal cancer. *Chinese Journal of Digestive surgery.* 2019;08:797–802.

Figures

Figure 1

Superior rectal vein (red arrow).

Figure 2

Kaplan–Meier curves for metastasis-free survival (A), disease-free survival (B), and overall survival (C). SRV= superior rectal vein.