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Elective Colorectal Cancer Resection during Nighttime Hours is Clinically Acceptable

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ABSTRACT

Purpose: This study aimed to compare the perioperative and survival outcomes of elective colorectal cancer resection performed during daytime versus nighttime hours to determine if nighttime surgery yields comparable results.

Methods: We retrospectively reviewed the clinical data of 265 patients, categorizing them into nighttime or daytime groups based on surgery start and end times. Baseline characteristics were compared. Risk factors for perioperative complications, progression-free survival (PFS), and overall survival (OS) were analyzed, along with PFS and OS between groups.

Results: The median follow-up was 46 months (range: 0–48). Of the 265 patients, 69 (26.0%) underwent nighttime surgery. No significant differences were observed in baseline characteristics or perioperative outcomes between groups ($P > 0.05$). Adjusted logistic regression identified a primary lesion diameter ≥50 mm as an independent risk factor for perioperative complications (OR: 2.24, 95% CI: 1.09–4.60). Timing of surgery was not significantly associated with complications (OR: 0.99, 95% CI: 0.53–1.85). Nighttime surgery did not significantly affect PFS (HR = 1.00, 95% CI: 0.55–1.82, P = 0.995) or OS (HR = 0.63, 95% CI: 0.27–1.45, P = 0.277).

Conclusion: Nighttime elective colorectal cancer resection demonstrates similar short-term safety and long-term survival outcomes compared to daytime surgery. Nighttime surgery may be considered when daytime operating capacity is insufficient.

Keywords: Nighttime surgery; Colorectal cancer; Short-term outcomes; Survival

INTRODUCTION

Colorectal cancer (CRC) ranks as the second most common malignancy in men and the fourth in women [1]. Enterectomy with regional lymph node dissection remains a primary treatment for non-advanced CRC. In many high-volume centers, an increasing surgical load necessitates performing a substantial number of CRC procedures during nighttime hours. While some studies suggest a higher frequency of adverse events and worse postoperative outcomes for nighttime surgeries [2-6], others reported no association between nighttime surgery and perioperative complications [7-14]. However, these studies largely focused on emergency or transplant surgeries and did not include patients undergoing elective radical resection for CRC. To date, no study has specifically evaluated the perioperative safety and survival outcomes of nighttime elective radical resection for CRC. This study aimed to investigate whether performing elective radical CRC resection during nighttime hours impacts perioperative safety and oncological survival.

MATERIALS AND METHODS

Patients

We conducted a retrospective analysis of consecutive CRC patients who underwent radical resection at Zhejiang Cancer Hospital between September 2020 and December 2020. Inclusion criteria were: (a) pathological confirmation of CRC; (b) performance of enterectomy with regional lymph node dissection; and (c) availability of complete clinic-pathological, surgical, and hospitalization records. Exclusion criteria were: (a) emergency surgery; (b) operations spanning both daytime and nighttime periods; and (c) procedures without regional lymph node dissection. Finally, 265 patients were included (Figure 1). Based on surgery start and end times, patients were categorized into a daytime surgery (DTS) group or a nighttime surgery (NTS) group.

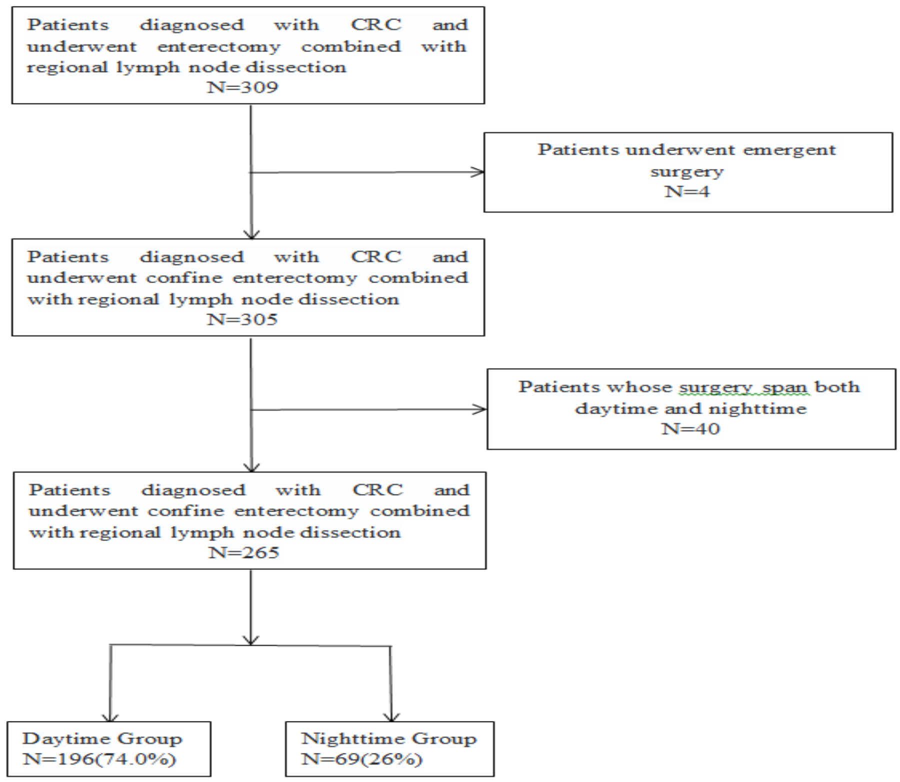

Figure 1: Patients screening flow

Definition of Nighttime and Daytime Surgery

Definition of nighttime and daytime were adapted with modifications based on a study focusing on elective nighttime surgeries [28]. Nighttime was defined as 6:00 PM to 8:00 AM, and daytime as 8:00 AM to 6:00 PM. Nighttime surgery (NTS) was defined as an operation starting after 6:00 PM and concluding before 8:00 AM the following morning. Daytime surgery (DTS) was defined as an operation starting after 8:00 AM and ending before 6:00 PM. The definition ensured that all nighttime procedures were conducted completely within the nighttime period, while nighttime procedures were carried out entirely at night. Nighttime surgeries were performed non-selectively due to high surgical volume exceeding daytime capacity. All surgeries were performed by six attending surgeons and their teammates, with each surgeon capable of completing over 200 CRC resection surgeries annually, which contributed to high surgical quality. All attending surgeons had completed a full daytime workload before commencing nighttime operations, and were not on night duty the day before surgery.

DATA COLLECTION

Demographic and clinical data were extracted from the hospital information system. Collected baseline characteristics included gender, age, tumor site, body mass index (BMI), diabetes, hypertension, other comorbidities, smoking history, alcohol use, prior abdominal surgery, preoperative tumor-related symptoms, neoadjuvant chemotherapy, neoadjuvant radiotherapy, primary lesion size, and ASA grade. Other comorbidities encompassed cardiovascular/cerebrovascular diseases, chronic lung disease, arrhythmia, dementia, hyperlipidemia, psychiatric disorders, electrolyte imbalances, hepatic/renal dysfunction, chronic urinary system diseases, malnutrition, and anemia.

Intraoperative outcomes recorded were adverse events (including hyperkalemia, massive hemorrhage, adjacent organ injury, fecal contamination, and cardiopulmonary/cerebrovascular accidents), estimated blood loss, transfusion requirement, surgical approach (laparoscopic vs. open), and operative time. Postoperative outcomes included complications, readmission, unplanned reoperation, postoperative length of stay, and hospitalization costs. Postoperative complications were defined as hospital-acquired infections, bleeding, anastomotic leak, hepatic/renal dysfunction, electrolyte imbalance, moderate-to-severe anemia, intestinal obstruction, and cardiopulmonary complications, and the timeframe for postoperative complications is defined as the period from surgery to 30 days postoperatively..

Statistical Analysis

Analyses were performed using SPSS 26.0. Baseline characteristics were compared using the chi-square test. Intraoperative and postoperative outcomes were compared using the chi-square test (categorical) and Student's t-test (continuous). Univariate and multivariate binary logistic regression analyses identified independent predictors of perioperative complications. Factors influencing progression-free survival (PFS) and overall survival (OS) were analyzed using Cox proportional hazards models. Survival curves for subgroups were generated using the Kaplan-Meier method. A P-value < 0.05 was considered statistically significant.

RESULTS

Follow-up

The study included 265 patients undergoing radical CRC resection. Among them, 196 (74.0%) and 69 (26.0%) underwent surgery during daytime and nighttime hours, respectively. The last follow-up date was September 30, 2024. The median follow-up was 46 months (range: 0–48), with a mean of 41.9 months (95% CI: 40.5–43.4). Comparison of Baseline Characteristics and Perioperative Outcomes

No significant differences were found between the DTS and NTS groups in any baseline clinical features (P > 0.05) (Table 1). Similarly, no significant differences were observed in intraoperative or short-term postoperative outcomes (P > 0.05) (Table 2).

Table 1: Comparison of baseline characteristics between NTS and DTS groups

Characteristics		DTS N=196(%)	NTS N=69(%)	P value
Gender				0.734
	Female	61(31.1)	23(33.3)	
	Male	135(68.9)	46(66.7)	
Age				0.462
	<70	156(79.6)	52(75.4)	
	>=70	40(20.4)	17(24.6)	
Site				0.307
	Rectum	159(81.1）	52(75.4)	
	Colon	37(18.9)	17(24.6)	

BMI				0.074
	<28	189(96.4)	62(89.9)	
	>=28	7(3.6)	73(10.1)	
Diabete				0.951
	No	171(87.2)	60 (87.0)	
	Yes	25(12.8)	9(13.0)	
Hypertension				0.782
	No	137(69.9)	47(68.1)	
	Yes	59(30.1)	22(31.9)	
Underlying diseases				0.835
	No	151(77.0)	54(78.3)	
	Yes	45(23.0)	15(21.7)	
Smoking				0.734
	No	121(61.7)	41(59.7)	
	Yes	75(38.3)	28(40.6)	
Drinking				0.471
	No	137(69.9)	45(65.2)	
	Yes	59(30.1)	24(34.8)	
Previous abdominal surgery				0.828
	No	148(75.5)	53(76.8)	
	Yes	48(24.5)	16(23.2)	
ASA Grade				0.276
	GradeI	103(52.6)	31(44.9)	
	GradeII	93(47.4)	38(55.1)	
Diameter of lesion				0.429
	<50mm	147(75.0)	55(79.7)	
	>=50mm	49(25.0)	14(20.3)	
Radiotherapy				0.783
	No	181(92.3)	63(91.3)	
	Yes	15(7.7)	6(8.7)	
Chemotherapy				0.363
	No	163(83.2)	54(78.3)	
	Yes	33(16.8)	15(21.7)	
Primary symptom				0.233
	No	173(88.3)	57(82.6)	
	Yes	23(11.7)	12(17.4)	

Table 2: Perioperative outcome comparison of DTS and NTS group

Outcomes		DTS	NTS	P value
		N=196(%)	N=69(%)	
Laparoscope				0.941
	No	9(4.6)	4(5.8)	
	Yes	187(95.4)	65(94.2)	
	Conversion to open laparotomy			0.463
	No	184(98.4)	63(96.9)	

	Yes	3(1.6)	2(3.1)	
Enterostomy				0.144
	No	88(44.9)	24(34.8)	
	Yes	108(55.1)	45(65.2)	
Blood loss				0.149
	<200ml	175(89.3)	57(82.6)	
	>=200ml	21(10.7)	12(17.4)	
Blood transfusion				0.979
	No	237(96.7)	58(96.7)	
	Yes	8(3.3)	2(3.3)	
Intraoperative adverse event				1
	No	193(98.5)	68(98.6)	
	Yes	3(1.5)	1(1.4)	
Operation time		162.3±67.0	167.4±73.8	0.398
Postoperative complications				0.844
	No	60(30.6)	22(31.9)	
	Yes	136(69.4)	47(68.1)	
Readmission				0.167
	No	195(99.5)	67(97.1)	
	Yes	1(0.5)	2(2.9)	
Re-operation				0.575
	No	192(98.0)	69(100.0)	
	Yes	4(2.0)	0(0)	
Hospitalization days after surgery				0.219
	<14 days	151 (77.0)	58(84.1)	
	>=14 days	45(23.0)	11(15.9)	
Total cost(thousand)		63.6±22.1	59.8±12.8	0.153

Risk Factor Analysis for Perioperative Complications

Univariate and adjusted multivariate logistic regression analyses identified a primary lesion diameter ≥50 mm as an independent risk factor for perioperative complications (adjusted OR: 2.24, 95% CI: 1.09–4.60) (Table 3). The timing of surgery (nighttime vs. daytime) was not significantly associated with perioperative complications (adjusted OR: 0.99, 95% CI: 0.53–1.85, P = 0.973) (Table 4).

Table 3: Comparison of risk factors between patients with or without perioperative complications

Characteristics		With complications N=82(100%)	Without complications N=183(100%)	P value
Gender				***0.01***
	Male	65(79.3)	116(63.4)	
	Female	17(20.7)	67(36.6)	
Age				0.068
	<70	70(85.4)	138(75.4)	
	>=70	12(14.6)	45(24.6)	

Site				0.815
	Rectum	66(80.5）	145(79.2)	
	Colon	16(19.5)	38(20.8)	
BMI				0.276
	<28	80(97.6)	171(93.4)	
	>=28	2(2.4)	12(6.6)	
Diabete				0.546
	No	73(89.0)	158 (86.3)	
	Yes	9(11.0)	25(13.7)	
Hypertension				0.552
	No	59(72.0)	125(68.3)	
	Yes	23(28.0)	58(31.7)	
Underlying diseases				0.147
	No	68(82.9)	137(74.9)	
	Yes	14(17.1)	46(25.1)	
Smoking				0.394
	No	47(57.3)	115(62.8)	
	Yes	35(42.7)	68(37.2)	
Drinking				0.07
	No	50(61.0)	132(72.1)	
	Yes	32(39.0)	51(27.9)	
Previous abdominal surgery				***0.035***
	No	69(84.1)	132(72.1)	
	Yes	13(15.9)	51(27.9)	
ASA Grade				0.347
	GradeI	45(54.9)	89(48.6)	
	GradeII	37(45.1)	94(51.4)	
Diameter of lesion				***0.019***
	<50mm	70(85.4)	132(72.1)	
	>=50mm	12(14.6)	51(27.9)	
Radiotherapy				0.219
	No	78(95.1)	166(90.7)	
	Yes	4(7.7)	17(9.3)	
Chemotherapy				0.523
	No	69(84.1)	148(80.9)	
	Yes	13(15.9)	35(19.1)	
Primary symptom				0.133
	No	75(91.5)	155(84.7)	
	Yes	7(8.5)	28(15.3)	
Operative time				0.844
	Daytime	60(73.2)	136(74.3)	
	Nighttime	23(26.8)	47(25.7)	

Table 4: Logistics regression analysis of risk factors for perioperative complications

Variable	Univariable OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Gender	0.45(0.25-0.86)	***0.01***	0.55(0.28-1.10)	0.093
Age	1.90(0.95-3.83)	0.07	1.72(0.84-3.53)	0.142
Primary Site	1.08(0.56-2.08)	0.82	-	-
BMI	2.81(0.61-12.84)	0.18	-	-
Diabete	1.28(0.57-2.89)	0.55	-	-
Hypertension	1.19(0.67-2.11)	0.55	-	-
Underlying diseases	1.63(0.84-3.17)	0.15	-	-
Smoking	0.79(0.47-1.35)	0.39	-	-
Drinking	0.61(0.35-1.05)	0.07	0.72(0.39-1.33)	0.29
Previous abdominal surgery	2.05(1.04-4.03)	***0.04***	1.67(0.81-3.44)	0.163
ASA Grade	1.29(0.76-2.17)	0.35	-	-
Diameter of lesion	2.25(1.13-4.50)	***0.02***	2.24(1.09-4.60)	***0.029***
Radiotherapy	2.00(0.65-6.13)	0.23	-	-
Chemotherapy	1.26(0.63-2.52)	0.52	-	-
Primary symptom	1.94(0.81-4.63)	0.14	-	-
Timing of operation (DT/NT)	0.94(0.52-1.70)	0.84	0.99(0.53-1.85)	0.973
Operation time(minutes)	1.00(1.00-1.01)	0.051	1.00(1.00-1.01)	0.139

Prognostic Factors for PFS and OS Cox multivariate analysis identified age and preoperative chemotherapy as independent prognostic factors for PFS (Table 5). For OS, preoperative tumor-related symptoms and preoperative chemotherapy were independent prognostic factors (Table 6).

Table 5: Cox Proportional Hazards Model analysis for PFS

Variable	Univariable HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Gender	1.24(0.72-2.14)	0.45	-	
Age	0.26(0.10-0.73)	***0.01***	0.32(0.11-0.89)	***0.029***
Primary Site	0.78(0.38-1.60)	0.5	-	
BMI	1.83(0.73-4.58)	0.2	-	
Diabete	0.67(0.27-1.69)	0.4	-	
Hypertension	1.04(0.59-1.84)	0.9	-	
Underlying diseases	1.67(0.94-2.96)	***0.08***	1.11(0.60-2.06)	0.748
Smoking	0.80(0.46-1.39)	0.42	-	
Drinking	0.91(0.51-1.62)	0.74	-	
Previous abdominal surgery	0.96(0.52-1.79)	0.9	-	
ASA Grade	1.40(0.82-2.39)	0.21	-	
Diameter of lesion	0.99(0.53-1.85)	0.98	-	
Radiotherapy	2.25(1.06-4.77)	***0.03***	0.83(0.33-2.07)	0.684
Chemotherapy	3.33(1.92-5.88)	***<0.001***	3.04(1.50-6.16)	***0.002***
Primary symptom	1.98(1.05-3.76)	***0.04***	1.86(0.96-3.61)	0.067
Timing of operation (DT/NT)	1.07(0.59-1.93)	0.83	1.00(0.55-1.82)	0.995
Operation time(minutes)	1.78(1.04-3.02)	***0.03***	1.44(0.83-2.52)	0.198

Table 6: Cox Proportional Hazards Model analysis for OS

Variable	Univariable HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Gender	0.77(0.37-1.58)	0.47	-	-
Age	0.84(0.37-1.90)	0.67	-	-
Primary Site	0.58(0.23-1.49)	0.26	-	-
BMI	1.61(0.50-5.24)	0.43	-	-
Diabete	1.65(0.73-3.74)	0.23	-	-
Hypertension	1.92(1.01-3.63)	***0.046***	1.86(0.96-3.59)	0.066
Underlying diseases	1.91(0.98-3.74)	0.06	1.09(0.53-2.21)	0.82
Smoking	1.02(0.53-1.95)	0.96	-	-
Drinking	1.00(0.50-1.98)	>0.99	-	-
Previous abdominal surgery	0.86(0.40-1.88)	0.71	-	-
ASA Grade	1.61(0.85-3.13)	0.14	-	-
Diameter of lesion	0.84(0.38-1.83)	0.66	-	-
Radiotherapy	4.99(2.42-10.28)	***<0.001***	1.54(0.61-3.90)	0.82
Chemotherapy	5.51(2.92-10.42)	***<0.001***	4.69(2.04-10.81)	***<0.001***
Primary symptom	2.21(1.04-4.66)	***0.04***	2.66(1.20-5.86)	***0.016***
Timing of operation (DT/NT)	0.89(0.42-1.87)	0.75	0.63(0.27-1.45)	0.277
Operation time(minutes)	2.09(1.11-3.96)	***0.02***	1.35(0.68-2.67)	0.392
Hemorrhage	2.40(1.14-50.80)	***0.02***	1.58(0.68-3.68)	0.286

Comparison of PFS and OS Between Subgroups

Patients aged ≥70 years had a lower risk of disease progression than those <70 years (HR = 0.32, 95% CI: 0.11–0.89, P = 0.029), with median PFS of 45.3 months (95% CI: 42.8–47.9) vs. 39.6 months (95% CI: 37.5–41.7, P = 0.005) (Figure 2a). Patients receiving preoperative chemotherapy had a higher risk of progression than those who did not (HR = 3.04, 95% CI: 1.50–6.16, P = 0.002), with median PFS of 31.8 months (95% CI: 26.1–37.4) vs. 42.8 months (95% CI: 41.2–44.5, P < 0.001) (Figure 2b). Surgery timing did not significantly affect PFS (HR = 1.00, 95% CI: 0.55–1.82, P = 0.995). Median PFS was comparable between the NTS (40.5 months, 95% CI: 37.0–44.0) and DTS groups (40.9 months, 95% CI: 38.9–43.0, P = 0.830) (Figure 2c). Patients with preoperative tumor symptoms had a higher risk of death than those without (HR = 2.66, 95% CI: 1.20–5.86, P = 0.016), with median OS of 39.1 months (95% CI: 33.9–44.3) vs. 43.8 months (95% CI: 42.3–45.3, P = 0.033) (Figure 2d). Similarly, patients receiving preoperative chemotherapy had a higher risk of death (HR = 4.69, 95% CI: 2.04–10.81, P < 0.001), with median OS of 34.3 months (95% CI: 29.2–39.4) vs. 45.2 months (95% CI: 43.9–46.4, P < 0.001) (Figure 2e). Again, surgery timing did not significantly affect OS (HR = 0.63, 95% CI: 0.27–1.45, P = 0.28). Median OS was similar between the NTS (43.4 months, 95% CI: 40.4–46.4) and DTS groups (43.1 months, 95% CI: 41.4–44.8, P = 0.750) (Figure 2f).

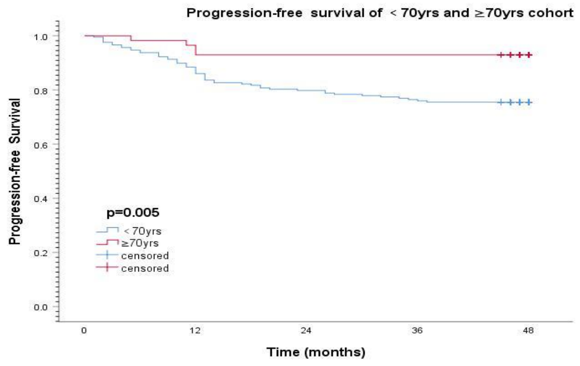

Figure 2a: Comparison of Figure 2a Pregression-free survival of patients elder or younger than 70 years old

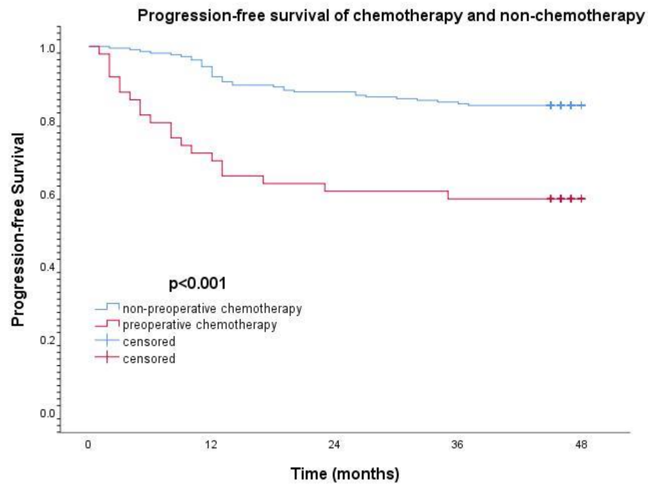

Figure 2b: Comparison of Pregression-free survival of patients with and without preoperative chemotherapy

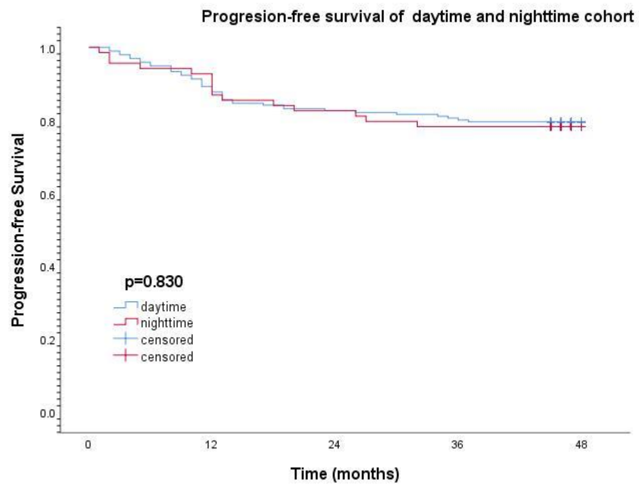

Figure 2c: Comparison of Progression-free survival of daytime and nighttime surgery group

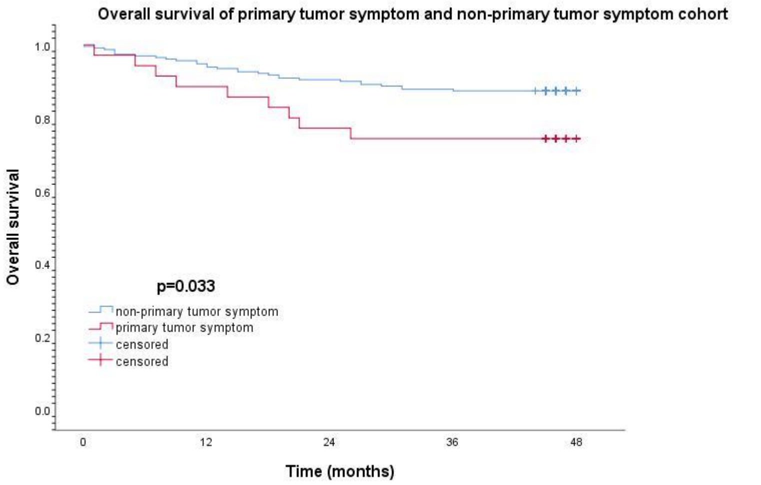

Figure 2d: Comparison of Overall survival of patients with and without primary tumor symptoms

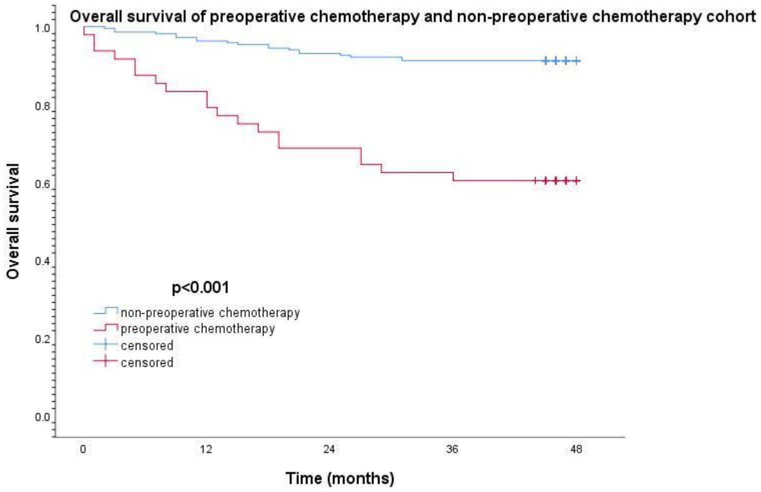

Figure 2e: Comparison of Overall survival of patients with and without preoperative chemotherapy

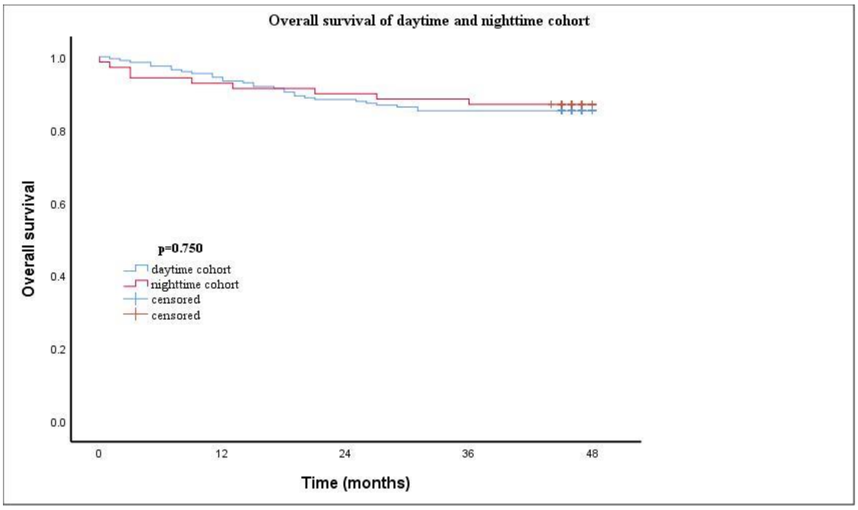

Figure 2f: Comparison of Overall survival of daytime and nighttime surgery group

DISCUSSION

In this study, the nighttime and daytime surgery groups demonstrated good comparability, as no significant differences were found in baseline characteristics. Our analysis confirmed that preoperative chemotherapy was independently associated with worse PFS and OS, whereas age ≥70 years correlated with improved PFS. A primary tumor size ≥5 cm was an independent predictor of perioperative complications. Importantly, the timing of surgery (nighttime vs. daytime) had no significant impact on either perioperative complications or survival outcomes.

The adverse impact of preoperative chemotherapy likely reflects the more advanced tumor stage or high-risk features (e.g., advanced T stage, nodal metastasis, vascular invasion, poor differentiation) in patients requiring neoadjuvant treatment, indicating inherently more aggressive tumor biology and poorer prognosis [15,16]. This aligns with indications for preoperative therapy outlined in major CRC guidelines[17-19]. The improved PFS observed in patients aged ≥70 years may be partially explained by an age-related decline in cellular proliferation rates, potentially reducing the accumulation of aggressive clones [20]. Furthermore, our finding that larger tumor size predicts higher perioperative complication risk is consistent with prior literature [21-24].

In agreement with several previous reports [3,8-10,13,14,25-27], we found no independent association between nighttime surgery and complication rates. However, direct comparison is limited as prior studies primarily involved emergency or transplant surgeries, where postponement often carries greater risk than nocturnal operation.

Our finding that nighttime surgery did not increase perioperative complication risk in elective CRC resection differs from some studies on other specialties [3,6]. Research on video-assisted thoracoscopic pulmonary resection or neurosurgery concluded that nighttime surgery increases complication risk, possibly because these procedures more frequently involve vital structures (e.g., brain, brainstem, major nerves, lungs, heart, great vessels) [3,6]. For instance, vascular injury was the predominant complication in thoracic series [6]. Similarly, a study on tissue-expander insertion for breast reconstruction reported increased risks for major complications requiring reoperation/readmission or expander removal in nighttime cases [28]. However, definitional differences exist, as that study focused on major complications, whereas we employed a broader complication definition. Surgeon fatigue is a recognized contributor to medical errors [29-31]. Studies indicate increased fatigue and perceived performance decline during nighttime hours following daytime work [32,33]. Fernandes et al. reported that 66.6% of sleep-deprived surgeons on emergency night shifts rated themselves as 'very fatigued' or 'exhausted,' with nearly all perceiving diminished performance [14]. Crucially, that study involved emergency on-call surgeons with pre-shift sleep deprivation, whereas our attending surgeons had no prior night duty, mandated rest periods, and were performing elective procedures, likely sustaining better operative performance. Furthermore, while sleep deprivation impairs simple tasks, complex cognitive operations may remain functional initially [34], and medical error rates do not always directly correlate with adverse event rates [35]. Therefore, based on our analysis, nighttime elective CRC resection appears acceptable in terms of short-term perioperative outcomes.

Our study also indicates that nighttime elective radical CRC resection does not adversely affect long-term oncological outcomes. Several factors may contribute to this finding. First, all procedures were performed by high-volume (≥200 annual cases), consistently composed surgical teams, ensuring technical uniformity. Second, attending surgeons were senior specialists without prior night shifts, and most had intervals between cases, minimizing fatigue from sleep deprivation and potentially contributing to precise tumor resection. Finally, our center maintains a dedicated, protocol-driven follow-up system, ensuring high-quality data collection. To our knowledge, this is the first study to evaluate the impact of surgery timing on survival for elective CRC resection, providing evidence against its clinical relevance. Furthermore, our strict definition of nighttime/daytime surgery, excluding procedures spanning both periods, may reduce bias, as CRC resections are lengthy and patients classified as daytime surgery in other studies might have actually concluded during nighttime hours. Our comprehensive analysis suggests that tumor characteristics, rather than operative timing, are the primary determinants of oncological outcomes in elective CRC resection. Despite its novelty, this study has limitations, including its retrospective design, potential unmeasured confounders, and single-center cohort. As no prior studies have specifically investigated nighttime elective CRC surgery's impact on survival, we believe larger, prospective, multi-center studies are warranted to further explore its effects on perioperative complications and oncological prognosis. Future research should also consider quantitative assessments of surgeon fatigue.

CONCLUSION

In summary, nighttime elective radical CRC resection demonstrates comparable short-term safety and long-term oncological outcomes to daytime surgery. Performing elective CRC resection during nighttime hours may be a feasible strategy when daytime operating capacity is exceeded, particularly in settings with high surgical demand or relatively scarce medical resources.

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DATA AVAILABILITY DECLARATION

The data supporting this study cannot be made publicly available due to privacy reason. However, they may be provided by the corresponding author upon reasonable request and subject to a data sharing agreement.

CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

AUTHOR CONTRIBUTIONS STATEMENT

Jun Luo, Zitong Wang, and Jing Lai wrote the primary main manuscript text; Zhibin Fang, Meijuan Zhu, and Chaojing Zheng collected the clinical data and did the follow up work; Yunxiao Liu and Chunlin Wang analyse the primary data; Nana Zhang and Jun Luo prepared figures; Meng Wang, Qian Zhang, and Yong Liu prepared the tables; Haiyang Feng, Yuping Zhu and Guiyu Wang revised the primary manuscript ; Jun Luo and Guiyu

Wang designed the project; Guiyu Wang revised the final version of the paper. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was conducted according to the principles expressed in the Declaration of Helsinki. Our research has been submitted to the Ethics Committee of Zhejiang Cancer Hospital and has been approved to be exempt from ethical review. Due to the retrospective study design, the informed consent was waived by the Ethics Committee of the Zhejiang Cancer Hospital.

CONSENT FOR PUBLICATION

Not Applicable.

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