

The start of gastrectomy at different time-of-day influences postoperative outcomes

Bin Wang, MM, Yizhou Yao, MM, Xuchao Wang, MM, Hao Li, MB, Huan Qian, MB, Linhua Jiang, MM, Xinguo Zhu, MD*

Abstract

Gastric cancer (GC) continues to be 1 of the malignant tumors with high morbidity and mortality worldwide. Although the improvements in targeted inhibitor therapy have promoted survival, the first choice for GC patients is still surgery. However, prolonged surgery may tire surgeons and affect surgical outcomes.

To detect whether different time-of-day radical gastrectomy influenced short-term and long-term surgical outcomes.

This study included 117 patients between 2008 and 2012 who underwent a radical gastrectomy. These patients were grouped into the morning (before 13:00) and afternoon (after 13:00) groups or divided into 2 groups according to the median operation start time (before or after 11:23). Then, the relevant influence of the surgical start time was analyzed.

The morning group (before 13:00) and the front median group (before 11:23) showed longer operative time ($P = .008$ and $P = .016$, respectively), lower estimated blood loss ($P < .001$ and $P = .158$, respectively), and longer time before resuming oral intake ($P < .001$ and $P < .173$, respectively) than the afternoon group (after 13:00) or latter median group (after 11:23). Starting the operation in the morning had no effect on the rate of postoperative complications. The operation start time had no significant influence on the overall survival of patients who underwent a radical gastrectomy. However, in subgroup analysis, patients who underwent a distal gastrectomy faced poor prognosis when their surgery started after 13:00 ($P = .030$).

The results suggest that the operation start time might be an indicator of total operative time, estimated blood loss, and the time to resuming oral intake. The operation start time may also influence the prognosis of radical gastrectomy in patients with GC.

Abbreviations: ASA = American Society of Anesthesiologists, GC = gastric cancer, OS = overall survival, pTNM = pathological TNM, TNM = tumor node metastasis.

Keywords: gastric cancer, operation start time, overall survival, perioperative indicators

1. Introduction

Gastric cancer (GC) is a kind of gastrointestinal malignancy with high morbidity and mortality. A total of 18.1 million new cases and 9.6 million cancer deaths occurred worldwide during 2018.

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Department of General Surgery, The First Affiliated Hospital of Soochow University, Suzhou, China.

* Correspondence: Xinguo Zhu, Department of General Surgery, The First Affiliated Hospital of Soochow University, Suzhou 215006, China (e-mail: xgzhu45@163.com).

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The number of new cases of GC in 2019 is estimated to be about 1.03 million and holds sixth place in the number of new cancer cases. More than half of all the new cases and deaths will occur in Asia.^[1,2]

In China, many GC patients present at the clinic at an advanced stage or with metastasis. The technical and physical requirements of surgeons are high. However, Chinese surgeons usually need to complete more than 2 operations a day and the total operative time is long. Thus, this tests the physical strength of the surgeons and the surgeon's workload can be considerable.

The biggest factor in human error has recently been attributed to doctors' fatigue, which led to the enactment of work-hours limitations.^[3] The work-hours limitations were brought into force in July 2003. The Accreditation Council for Graduate Medical Education recommended that work time should be limited to no more than 80 hours per week. Nevertheless, relevant research found that more than half of the medical workers work more than 80 hours a week.^[4]

Long working hours can lead to lack of sleep and fatigue in surgeons. Fatigue may result in loss of attention and affect surgical outcomes. Some studies suggest that technical skills may change at different time of the day. Therefore, fatigue and changes in the circadian rhythm of a doctor may decrease technical ability at different time.^[3] In recent research, the time-of-day is linked to prognosis after elective surgery,^[5,6] especially in general surgery, vascular surgery, and cardiac surgery.^[5,7-9] However, other studies have reported different results.^[10,11]

At present, there is a lack of research on the correlation between the start time and the outcome of radical gastrectomy for GC. We hypothesized that the outcome of radical gastrectomy would vary with different surgical start time. The present study aimed to compare the operative and survival outcomes of patients who underwent radical gastrectomy at different start time.

2. Method

2.1. Case selection and data acquisition

A retrospective cohort study of 117 patients who underwent radical gastrectomy in the First Affiliated Hospital of Soochow University from 2008 to 2012 was investigated (Fig. 1). All the information was collected from the Haitai electronic medical record database and the electronic anesthesia records. The definition of the start of surgery was the commencement of the operation (knife to skin) and the end of the operation was closing the incision. We categorized the start time according to the median time (before or after 11:23, the median start time) or 13:00 (operating room schedule 09:00–17:00). All cases were performed from Monday through Friday. Patients who received chemotherapy or radiotherapy, were emergency cases, were cachexic, or were multiple-organ resection cases were excluded. The Ethics Committee of The First Affiliated Hospital of Soochow University approved this study. Because the data were collected from the electronic medical records and had no

personally identifiable information, the requirement to obtain informed consent was waived.

2.2. Peri-operative contrast indicators

To clarify the difference between the morning group and the afternoon group, perioperative indicators were compared. These included intraoperative complications (intraoperative organ injury rate), postoperative complications (abdominal abscess, anastomotic fistula, anastomotic stenosis, intestinal obstruction, gastroparesis, dumping syndrome, and postoperative gastric bleeding), postoperative hospitalization time, operation duration, estimated blood loss, preoperative and postoperative white blood cell count, and albumin count. The compared indices also included the patients' gender, age, American Society of Anesthesiologists (ASA) score, tumor location, tumor size, and tumor node metastasis (TNM) stage. The TNM stage for GC was analyzed according to the 8th Edition of The American Joint Committee on Cancer Staging Manual. These covariables can help remove confounding bias at a later stage.

2.3. Statistical Analyses

The numerical data between the 2 groups were analyzed via Student *t*-tests. The classified data were calculated by the chi-squared test. The data were represented as the mean plus or minus the standard deviation for numerical variables and the

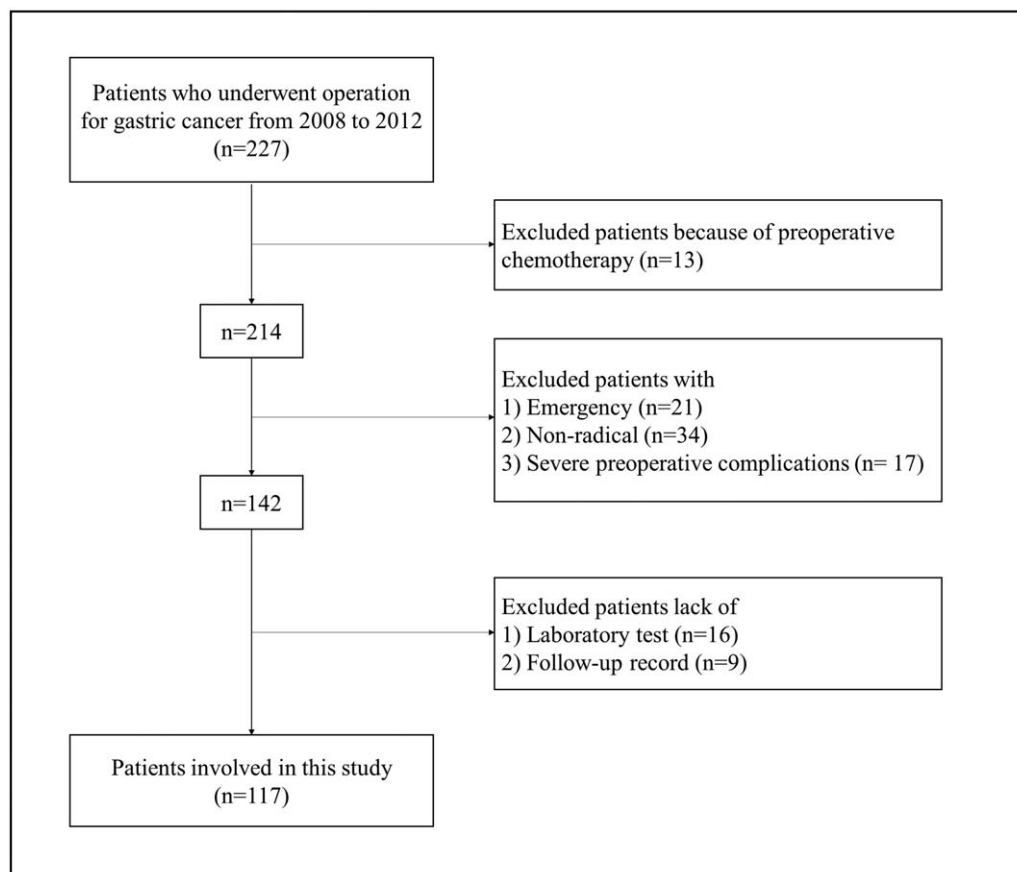


Figure 1. Flow diagram of the patients analyzed.

Table 1**Correlation analysis of the preoperative characteristics and operation start times.**

Characteristics	≤13	>13	P-value	≤median	≥median	P-value
Gender			.851			.137
Male	65	25		42	48	
Female	19	8		17	10	
Age (yr)			.802			.146
<65	31	13		28	18	
≥65	53	20		33	40	
Previous abdominal surgery			.492			.224
Yes	23	7		18	12	
No	61	26		41	46	
Hypertension			.608			.254
Yes	27	9		21	15	
No	57	24		38	43	
Preoperative ALB (g/L)			.742			.348
<35	18	8		11	15	
≥35	66	25		48	43	

ALB=albumin.

percentage of nominal variables. P -values $<.05$ indicated significant difference. SPSS 22.0 was used for the statistical analyses.

3. Results

3.1. Baseline and pathological characteristics

We conducted correlation analysis to investigate whether the baseline and pathological characteristics of the patients affected the surgeons' scheduled operation start time. The results are summarized in Tables 1 and 2. There was no significant difference between the morning and afternoon group for gender, age, previous abdominal surgery, hypertension, albumin, tumor size, tumor invasion, lymph node metastasis, pathological TNM, nerve invasion, or vascular invasion ($P >.05$).

3.2. Intraoperative outcomes

As the results in Table 3 show, the surgical start time exerted a significant impact on the duration of surgery and the operative time in the morning group was generally longer than that in the afternoon group, regardless of start time before or after 13:00 ($P = .008$), or median start time ($P = .016$). In addition, during the radical gastrectomies, patients in the afternoon group lost significantly more blood than those in the morning group ($P <.001$). No statistical difference was found in the ASA score and type of resection between the morning group and afternoon groups ($P >.05$).

To further analyze the relationship between the start time of surgery, the estimated intraoperative blood loss, and the duration of surgery, we calculated the variation in trends in the amount of blood loss and the duration of surgery in different operation start

Table 2**Pathological indicators.**

Characteristics	≤13	>13	P-value	≤median	>median	P-value
Tumor size (cm)			.060			.212
<5	61	18		43	36	
≥5	23	15		16	22	
Tumor differentiation			.577			.781
Well	43	15		30	28	
Poor	41	18		29	30	
Tumor invasion			.202			.878
T1-2	25	6		16	15	
T3-4	59	27		43	43	
Lymph node metastasis			.623			.629
Yes	50	18		33	35	
No	34	15		26	23	
pTNM			.841			.785
I-II	45	17		32	30	
III-IV	39	16		27	28	
Nerve invasion			.383			.360
Yes	30	9		22	17	
No	54	24		37	41	
Vascular invasion			.663			.360
Yes	29	10		22	17	
No	55	23		37	41	

pTNM= pathological TNM.

Table 3**Correlation analysis of operative characteristics and operation start times.**

Characteristics	≤13	>13	P-value	≤median	≥median	P-value
ASA			.559			.791
1-2	63	23		44	42	
3-4	21	10		15	16	
Type of resection			.458			.052
Distal gastrectomy	42	18		27	33	
Proximal gastrectomy	15	8		9	14	
Total gastrectomy	27	7		23	11	
Estimated blood loss (mL)	117.93±112.01	227.88±181.79	<.001	130.36±127.48	167.84±156.82	.158
Operating time	174.19±54.70	151.82±32.37	.008	178.93±54.64	156.64±43.14	.016

ASA=American Society of Anesthesiologists.

times. The analysis revealed that later operation start time was associated with more blood loss and the operative time tended to decrease gradually with later start time (Fig. 2A and B).

3.3. Postoperative outcomes

Table 4 lists the results of the correlation analysis of the postoperative characteristics and the operation start times. Interestingly, we observed that patients whose surgery started after 13:00 resumed oral intake later than patients with earlier surgical time ($P=.042$). However, this did not significantly affect postoperative complications. The length of stay in the hospital after surgery was similar in the morning and the afternoon groups and in the before and after median time groups.

3.4. Survival outcomes

In the prognosis analysis, we found that the overall survival (OS) between the morning and afternoon groups or between the before

and after median time groups were not significantly different (Fig. 3A and B). Subgroup survival analysis was also performed according to the type of resection and the total patients were divided into 3 subgroups. Contrary to our expectations, the afternoon distal gastrectomy group had a poorer prognosis than the morning group ($P=.030$) and the other subgroups did not differ from each other (Fig. 4A-F).

To further explore the reason behind the poorer prognosis in the afternoon distal gastrectomy group, we performed subgroup analysis. The entire cohort was subgrouped to reassess the risk and survival rates. The results indicated that OS was increased only in the distal gastrectomy morning surgery group and no other subgroups (Fig. 5).

4. Discussion

GC is associated with high morbidity and mortality worldwide.^[1] In addition to early GC and metastatic GC (TNM IV period), the most effective treatment for GC is still surgery.^[12-14] Many

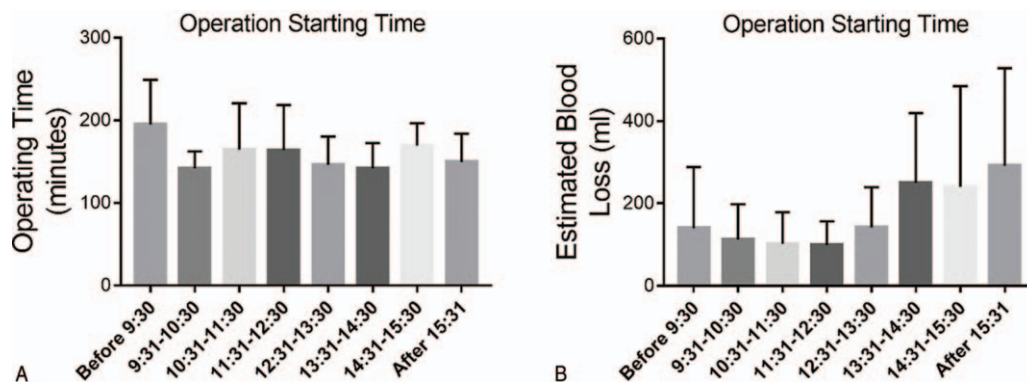


Figure 2. The trend in blood loss and the duration of surgery at different operation start times. (A) The relationship between operative duration and operation start time. (B) The relationship between the amount of blood loss and operation start time.

Table 4**Correlation analysis of postoperative characteristics and operation start times.**

Characteristics	≤13	>13	P-value	≤median	>median	P-value
Postoperative complication			.738			.975
Positive	8	4		6	6	
Negative	76	29		53	52	
Time of resuming oral intake	4.10±1.34	4.67±1.38	.042	4.08±1.34	4.43±1.39	.173
Postoperative stay (d)	10.96±4.57	11.58±6.04	.555	11.15±4.41	11.12±5.59	.973

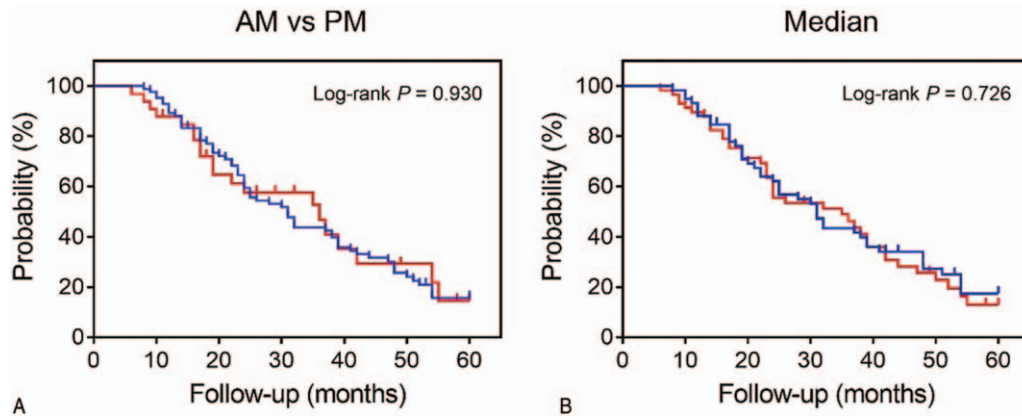


Figure 3. The Kaplan-Meier survival analysis of OS for the effect of operation start time. (A) Patients grouped before 13:00 (AM) and after 13:00 (PM) (B) Patients divided into 2 groups according to the median operation start time (before and after 11:23). The blue curve represents surgery started in the morning and the red curve represents surgery started in the afternoon.

patients with GC are diagnosed at an advanced stage, which enhances the complexity of surgery to some degree. Workload and surgical complexity have been shown to contribute to surgeon fatigue. Because surgeon fatigue may affect surgical outcomes, this study aimed to analyze whether the outcomes of radical gastrectomy were related to surgical start time.

To explore whether start time was related to surgical outcomes, we analyzed the correlation between the surgical

start time and intraoperative conditions, postoperative complications, and prognosis. The results revealed no statistical difference between the general condition and pathological features of the different time-of-day surgeries.

Similar to the results of previous studies, the start time of surgery had a significant impact on the duration of surgery and the operative time in the morning group was usually longer than in the afternoon group.^[3,5,7,9] This may suggest that there is

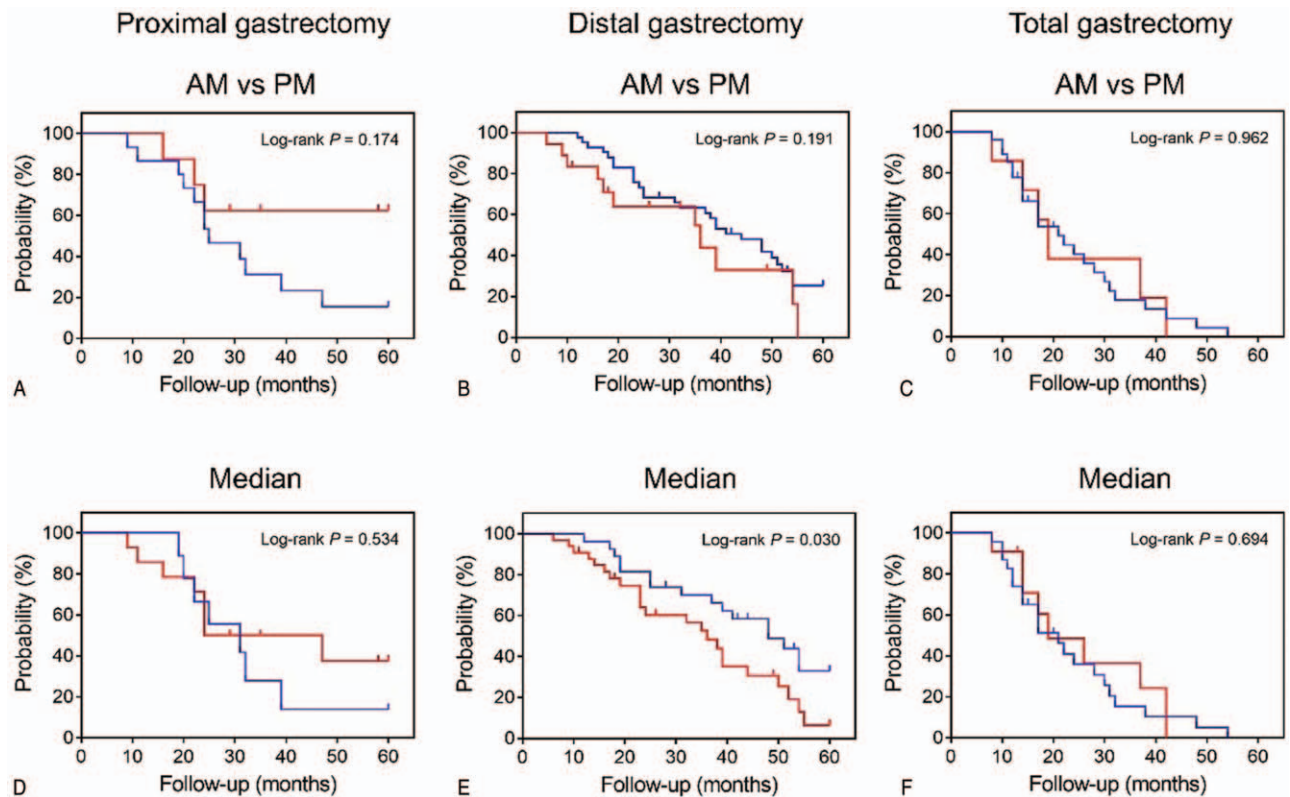


Figure 4. Kaplan-Meier subgroup survival analysis according to different types of gastrectomy. The patients were grouped before 13:00 (AM) and after 13:00 (PM) and divided into 2 groups according to the median operation start time. (A–D) Proximal gastrectomy. (B–E) Distal gastrectomy. (C–F) Total gastrectomy. The blue curve represents surgery started in the morning and the red curve represents surgery started in the afternoon.

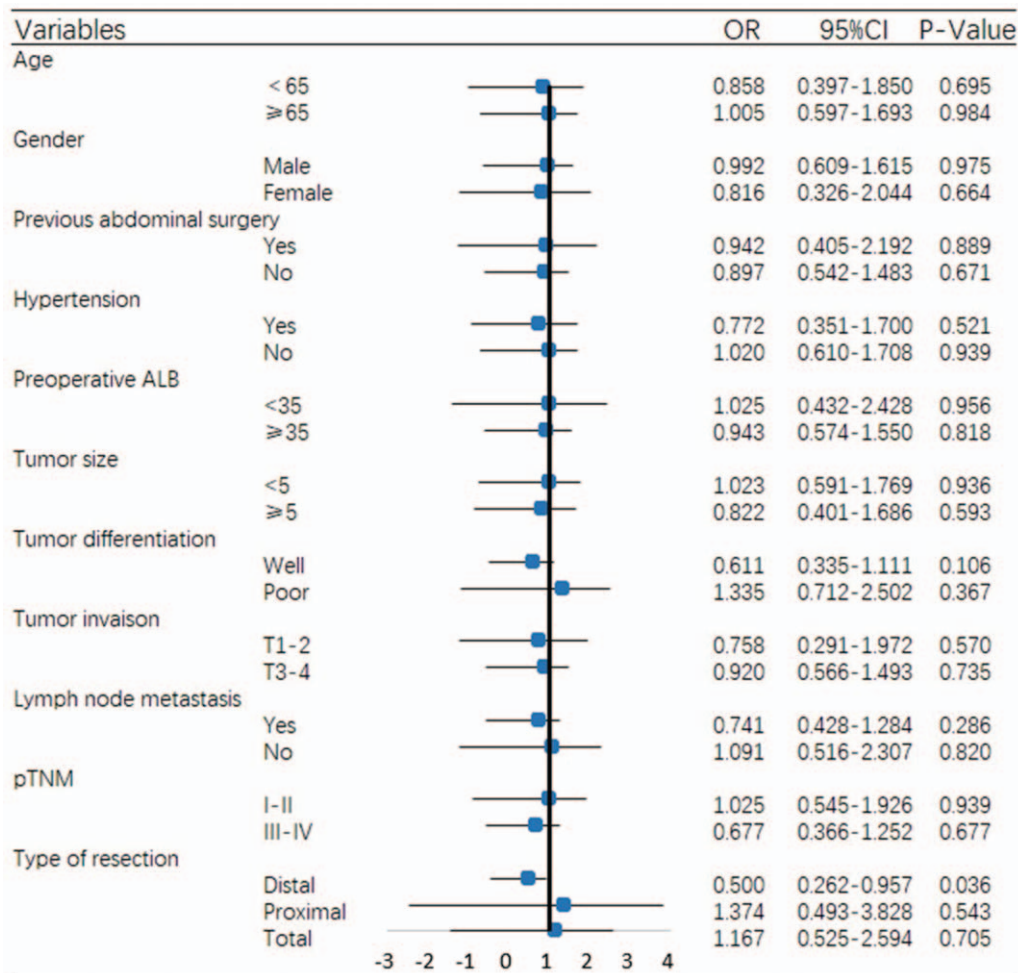


Figure 5. Subgroup analysis for factors influencing the duration of overall survival of gastrectomy patients according to operation start time.

usually only 1 major operation scheduled in the morning. Surgeons may also feel more energetic and pace their procedure to use the available time (ie, more time available in the morning due to fewer procedures than in the afternoon). In addition, the estimated blood loss was generally higher in the afternoon group and patients who received surgery in the afternoon generally needed longer time to resume oral intake.

In our hospital, the operating room nurses take over for the daily workgroup at 17:00. In principle, the operating room schedule should not affect the surgeons, however, the surgeons might be affected by the psychological hint—“to rush to finish the operation” to some degree by the shift in nurses. In addition, no noon break might be an important reason for the perioperative differences related to fatigue of the surgeons in the afternoon. Lack of sleep and fatigue affect hand-eye coordination.^[15-17] Sleep deprivation and fatigue can be caused by extended working hours and circadian rhythm disorders.^[18-20] It has been reported that in general surgery, neurosurgery, cardiac surgery, orthopedics and gynecology, the surgical start time and operative time had significant impacts on the surgical results, which was largely attributed to the fatigue of the surgeons and changes in human circadian rhythm.^[21,22]

However, the duration of postoperative hospitalization was similar between the morning and afternoon groups. And in the

prognosis analysis, no difference in OS was found between the 2 groups. However, in subgroup survival analysis performed according to the type of resection, the OS of distal gastrectomy patients in the afternoon group was poorer and there was no difference between the other groups. Previous studies have suggested that differences in operation start time and the duration of surgery did not affect patient prognosis.^[10,11,23] However, the results of the subgroup analysis in this study suggested that the start time of surgery may play an important role in prognosis. However, there were some limitations to this study. First, the outcome may also be related to the small sample size of the study. We avoided surgical techniques and treatment bias by including patients in the fixed treatment teams, but this led to insufficient sample size. Second, the number of operations a surgeon performed in 1 weekday was not listed as a parameter in this study and the performance of other team members, like fellows and nurses, was too difficult to include in the analyses. These limited the accuracy and significance of the subgroup analysis.

In summary, our results suggested that operation start time may influence surgical outcomes. Compared to patients who underwent radical gastrectomies in the morning, patients operated in the afternoon had more intraoperative blood loss, shorter operative time and longer recovery time of gastrointestinal function. There

was also a significant difference in OS in the subgroup comparison of distal gastrectomy patients.

Author contributions

Conceptualization: Xinguo Zhu.

Formal analysis: Linhua Jiang.

Investigation: Bin Wang, Yizhou Yao, Xuchao Wang, Hao Li, Huan Qian, Xinguo Zhu.

Methodology: Xinguo Zhu.

Writing – original draft: Bin Wang, Yizhou Yao, Xuchao Wang, Linhua Jiang, Xinguo Zhu.

Writing – review and editing: Bin Wang, Xinguo Zhu.

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