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Surgical staging of locally advanced colorectal cancer: A comparative analysis of diagnostic error rates across study groups

Abstract

Aim. To evaluate the additional diagnostic value of minimally invasive surgical verification in selected patients with indeterminate imaging results, rather than directly comparing two diagnostic strategies.

Materials and methods. A comprehensive analysis of staging results of 140 patients with morphologically verified T3-T4 colorectal cancer was performed. The study design was an observational retrospective-prospective cohort trial, approved by the local ethics committee. Patients were divided into three groups: a baseline control group with purely non-invasive imaging, a monodiagnostic group with one targeted minimally invasive intervention, and a combined surgical exploration group.

Results. Isolated radiological staging was accompanied by underdiagnosis of occult peritoneal carcinomatosis at a rate of 47.0% and overdiagnosis of reactive thoracic changes at 18.2%. The synergistic combination of methods increased diagnostic accuracy to 96.4% with a specificity of 98.2%. The postoperative complication rate was 6.3%, with no life-threatening conditions. The implementation of the algorithm was associated with a change in treatment strategy in 42.1% of patients, which allowed for precise restaging. The survival analysis results (HR = 0.64; 95% CI 0.43-0.96; $p = 0.032$) are interpreted as an unadjusted association and act as an exploratory secondary outcome.

Conclusions. Routine non-invasive modalities generate a massive amount of false conclusions. The application of minimally invasive exploration in selected patients allows for accurate staging clarification and is strongly associated with treatment strategy modifications.

Keywords: colorectal cancer; staging; peritoneal carcinomatosis; diagnostic laparoscopy; thoracoscopy; minimally invasive diagnostic techniques.

INTRODUCTION

Colorectal cancer (CRC) continues to be one of the most acute medical and social problems, with approximately 1.9 million new cases registered annually worldwide [1]. In Ukraine, this pathology also consistently holds a leading position in the structure of cancer incidence, which is confirmed by national epidemiological data [2]. The leading cause of cancer-related mortality in this pathology is metastatic disease, the risk of which is especially high at the T4 tumour stage [3]. The current paradigm of multimodal treatment for locally

advanced CRC is strictly determined by the status of distant spread; therefore, the success of therapy critically depends on the ability to identify the true extent of the tumour process even before the start of surgery [4]. The traditional diagnostic algorithm is based on routine non-invasive imaging methods, despite the fact that the weakest link of radiological diagnostics remains the identification of lesions less than 10 millimetres in diameter [5]. Objective gaps in radiology, which lead to fatal consequences in the form of exploratory

Suggested Citation:

Kolosovych I, Danylenko O. Surgical staging of locally advanced colorectal cancer: A comparative analysis of diagnostic error rates across study groups. *Med Sci Ukr.* 2026;22(3):54–59. DOI: <https://doi.org/10.32345/2664-4738.3.2026.05>

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laparotomies or unjustified denials of radical treatment, compel the use of minimally invasive surgical imaging methods *in vivo* [6-7].

The aim of this study was to evaluate the additional diagnostic value of minimally invasive surgical verification in selected patients with indeterminate imaging results, rather than to conduct a direct comparison of two diagnostic strategies during colorectal cancer staging.

MATERIALS AND METHODS

The study has a design of a retrospective-prospective observational cohort trial, which included 140 patients with colorectal cancer aged 29 to 81 years, with a mean age of 64.5 ± 10.4 years. The study was conducted in accordance with the requirements of the World Medical Association Declaration of Helsinki [8], with the written informed consent of the patients and with the approval of the local bioethics committee of the Bogomolets National Medical University (protocol No. 188 dated October 28, 2024). Inclusion criteria were patients with morphologically verified CRC with locally advanced T3-T4 tumours and suspicious areas for distant metastases according to primary screening data. Exclusion criteria included a decompensated stage of concomitant pathology, coagulopathy, and the first or second stages of the disease.

The distribution of patients into groups was not randomised, but was based on clinical feasibility and the results of the baseline examination. The first control group consisted of 45 patients, whose staging was performed exclusively by routine non-invasive methods (CT, MRI, PET-CT), since the radiological picture provided exhaustive and reliable criteria regarding the M-status. Patients with doubtful or indeterminate lesions requiring morphological confirmation were enrolled in the minimally invasive verification groups. The second monodiagnostic group included 67 patients

who underwent a single method of minimally invasive surgical diagnosis, in particular video-assisted thoracoscopy, mediastinoscopy, or diagnostic videolaparoscopy. The third combined diagnostic group was formed by 28 patients with polytopic indeterminate lesions that required a combination of several minimally invasive methods. Groups 2 and 3 were combined into a single minimally invasive verification cohort for survival analysis. Such merging is justified by the fact that both groups had a fundamentally common clinical characteristic – the presence of doubtful radiological imaging results, which *a priori* required surgical clarification. At the same time, group 1 consisted of patients whose imaging results were sufficiently definitive.

Baseline preoperative examination included contrast-enhanced CT of the chest, abdomen, and pelvis, MRI, and PET-CT [5, 9]. The surgical stage consisted of diagnostic videolaparoscopy with the calculation of the peritoneal cancer index (PCI), video-assisted thoracoscopic surgery (VATS), and cervical mediastinoscopy according to Carlens [7, 10]. The calculation of the operative characteristics of the methods was carried out by comparing their conclusions with the gold standard – the results of direct surgical exploration and pathomorphological examination. For patients in the first group, the reference standard for true negative results was data from dynamic clinical and radiological observation. Statistical processing was performed in the IBM SPSS environment using Student's t-test, Mann-Whitney U test, and chi-square test. Survival rates were calculated using the Kaplan-Meier method with significance testing via the Log-rank test.

RESULTS AND DISCUSSION

The median follow-up time for patients was 24 months. The baseline clinical and demographic characteristics of patients distributed by study groups are summarised in Table 1.

Table 1. Baseline clinical and demographic characteristics of patients by study groups (n = 140)

Indicator	Group 1 (n = 45)	Group 2 (n = 67)	Group 3 (n = 28)	Total (n = 140)
Mean age, years (M ± SD)	64.2 ± 10.6	64.7 ± 10.3	64.5 ± 10.1	64.5 ± 10.4
Gender (Male)	26 (57.8%)	39 (58.2%)	16 (57.1%)	81 (57.9%)
Gender (Female)	19 (42.2%)	28 (41.8%)	12 (42.9%)	59 (42.1%)
Localisation: Colon	27 (60.0%)	41 (61.2%)	18 (64.3%)	86 (61.4%)
Localisation: Rectum	18 (40.0%)	26 (38.8%)	10 (35.7%)	54 (38.6%)
Clinical stage: III	8 (17.8%)	26 (38.8%)	12 (42.9%)	46 (32.9%)
Clinical stage: IV	37 (82.2%)	41 (61.2%)	16 (57.1%)	94 (67.1%)
Histotype: Adenocarcinoma	27 (60.0%)	59 (88.1%)	19 (67.9%)	105 (75.0%)
Histotype: Mucinous/signet-ring	18 (40.0%)	8 (11.9%)	9 (32.1%)	35 (25.0%)
Metastases: Liver	25	30	15	70 (50.0%)
Metastases: Lungs	7	12	6	25 (17.9%)
Metastases: Peritoneum	0	10	7	17 (12.1%)
Metastases: Pleura	0	2	2	4 (2.9%)
Treatment: Polychemotherapy	32	36	25	93
Treatment: Radical resection	5	31	3	39
Treatment: Non-therap. laparotomy	8	0	0	8

Source: developed by the authors

A comparative analysis demonstrated the profound diagnostic inadequacy of an isolated radiological approach. The use of exclusively non-invasive methods led to a missed diagnosis of 47.0% of cases of occult peritoneal carcinomatosis and 51.4% of hidden metastases in the liver parenchyma, indicating a high rate of underdiagnosis [6, 11]. At the same time, the phenomenon of overdiagnosis was objectified, when hypermetabolic mediastinal lymph nodes or small pulmonary nodules detected on PET-CT had an exclusively inflammatory-reactive nature in 18.2% of cases. The transition to

minimally invasive exploration radically changed the picture of true dissemination. Diagnostic laparoscopy revealed 76.7% of clinically occult cases of peritoneal metastasis, completely neutralising the limitations of CT [7]. Morphological verification using mediastinoscopy and video-assisted thoracoscopy reliably refuted false diagnoses of generalisation and returned patients to the operable cohort [10]. Video-assisted thoracoscopy demonstrated a sensitivity of 96-99% and a specificity of 99%, while mediastinoscopy provided a sensitivity of 75% and a specificity of 98%.

Table 2. Comparative analysis of diagnostic error rates and staging accuracy by study groups

Indicator	Non-invasive imaging group (control)	Minimally invasive exploration groups
False-negative rate (missed peritoneal carcinomatosis)	47.0%	0% (neutralised)
False-positive rate (reactive thoracic changes)	18.2%	0% (refuted / down-staging)
Overall staging specificity	Suboptimal	98.2%
Overall diagnostic accuracy	Not evaluated as final	96.4%
Absolute risk reduction of futile laparotomies	Baseline risk	40%

Source: developed by the authors

Safety assessment of minimally invasive interventions showed that the overall total rate of postoperative complications (according to the Clavien-Dindo classification) among 95 patients in the exploration groups was only 6.3% [12]. The structure of complications was limited to the first and second grades, while life-threatening complications (Grade III-IV) and fatal outcomes (Grade V) were completely absent. Such safety allowed patients to initiate systemic polychemotherapy significantly faster compared to open exploratory laparotomies ($p < 0.001$). The implementation of this algorithm was

associated with a change in treatment strategy in 42.1% of patients. Such individualisation, based on histological M-status, allowed for clarification of staging and prevention of non-therapeutic surgical interventions. Figure 1 shows the Kaplan-Meier survival curves. The difference in survival ($HR = 0.64$; 95% CI 0.43-0.96; $p = 0.032$) between the control group and the minimally invasive verification groups is interpreted exclusively as an unadjusted association. Since the groups were non-randomised and formed based on clinical indications, this metric serves as an exploratory (secondary) outcome.

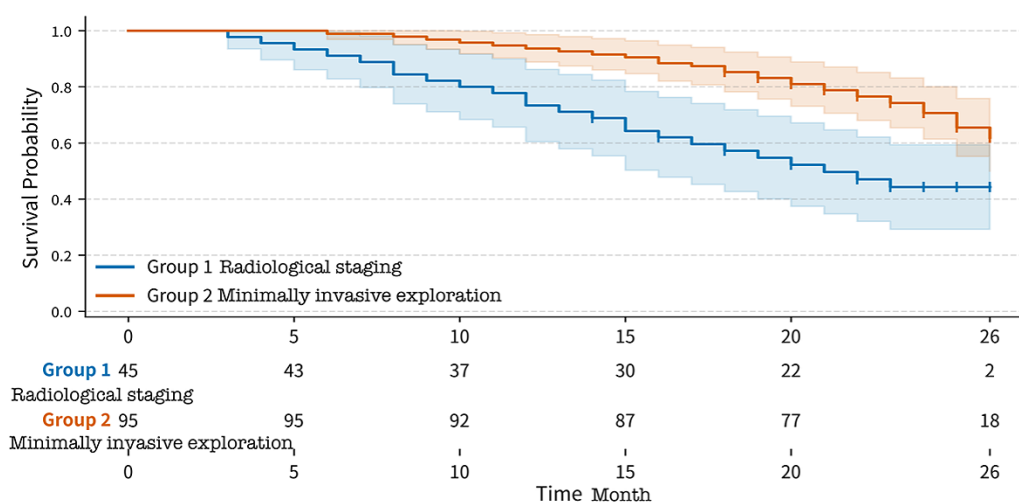


Figure 1. Kaplan-Meier survival curves

Note: demonstrating the difference between the radiological staging control group and the minimally invasive verification groups

Source: developed by the authors

Colorectal cancer progression is a complex cascade, where transserosal metastasis forms a growth pattern that often remains invisible to X-rays [13].

Recent epidemiological cohort studies indicate a clinically significant incidence of synchronous occult peritoneal spread, requiring a revision of standard staging

algorithms [14]. Furthermore, according to contemporary meta-analyses, the sensitivity of routine CT and MRI for detecting peritoneal metastases smaller than 10 mm remains critically suboptimal [15]. The obtained results confirm the limits of the diagnostic capacity of radiological imaging methods and point to an acute need for the involvement of minimally invasive surgery [9]. Minimally invasive verification revealed two opposite but equally dangerous phenomena of routine radiology. On the one hand, there is occult peritoneal carcinomatosis, which causes underdiagnosis and requires timely surgical up-staging to avoid futile laparotomies [11]. These data fully correlate with the conclusions of other authors who have proven that the integration of diagnostic laparoscopy safely detects micrometastases and significantly reduces the rate of open non-therapeutic exploration [16]. At the same time, the use of minimally invasive approaches minimises surgical stress response and immunosuppression compared to open laparotomy, which is recognised as a key factor for faster somatic recovery of patients in modern clinical guidelines [17]. On the other hand, hypermetabolic thoracic changes on PET-CT often turned out to be false positives, which allowed for down-staging in 18.2% of cases of thoracic findings. A similar phenomenon is described in detail in recent radiological studies, which confirmed that inflammatory and granulomatous reactions lead to intense non-specific uptake of 18F-FDG, creating a false picture of generalisation [18].

Although fine-needle aspiration (EBUS-TBNA) often serves as the modern standard for verifying mediastinal lymphadenopathy, the use of surgical mediastinoscopy ensured a full-fledged excisional biopsy yielding an intact lymph node. This was critically necessary for differentiating sarcoid-like reactions (paraneoplastic syndrome) from true tumour involvement. In the context of pulmonary dissemination, which is a frequent target of hematogenous metastasis, timely morphological differentiation using video-assisted thoracoscopy is vitally necessary to avoid overdiagnosis and to prescribe adequate systemic therapy [19]. Survival results require external confirmation using a multivariate Cox model, which would account for clinically relevant confounding factors [20]. For the final validation of the algorithm, it is advisable to conduct expanded multicentre studies [21]. Taken together, these

considerations highlight the need for a comprehensive diagnostic approach combining minimally invasive techniques, morphological verification and appropriate statistical adjustment to improve the accuracy and clinical applicability of the proposed algorithm.

CONCLUSIONS

1. The isolated use of non-invasive radiological imaging methods is accompanied by a critical rate of diagnostic errors, where the underdiagnosis rate of occult peritoneal carcinomatosis reaches 47.0%, and the overdiagnosis of reactive thoracic changes is 18.2%.

2. The integration of diagnostic videolaparoscopy, video-assisted thoracoscopy, and mediastinoscopy ensures diagnostic accuracy at the level of 96.4% with a minimal complication rate of 6.3%. The implementation of this approach was associated with a change in treatment strategy in 42.1% of patients and allowed for precise restaging.

3. The survival outcome (HR = 0.64) is an exploratory result and is interpreted as an unadjusted association requiring confirmation in future studies.

4. Study limitations should be considered when interpreting the results. Firstly, the non-randomised observational design carries a risk of selection bias. The key limitation is that groups were formed based on clinical indications related to the uncertainty of M-status, which creates a systematic difference between them as early as the baseline examination. A simple Kaplan-Meier analysis (log-rank test) does not allow attributing the difference in survival directly to the diagnostic strategy, since the patients potentially differ in stage and metastatic load. Secondly, the median follow-up time of 24 months is sufficient for analysing changes in clinical management, but assessing long-term survival requires further monitoring.

ACKNOWLEDGEMENTS

None.

FUNDING

The study was conducted using the institution's own resources, without the involvement of external funding sources.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Хірургічне стадіювання місцево-поширеного колоректального раку: порівняльний аналіз частоти діагностичних помилок у досліджуваних групах

Анотація

Мета. Оцінити додаткову діагностичну цінність малоінвазивної хірургічної верифікації у відібраних пацієнтів із невизначеними результатами візуалізаційних методів обстеження, замість прямого порівняння двох діагностичних стратегій.

Матеріали та методи. Проведено комплексний аналіз результатів стадіювання 140 пацієнтів із морфологічно підтвердженим колоректальним раком стадії Т3-Т4. Дизайн дослідження є спостережним ретро-проспективним когортним випробуванням, схваленим локальним етичним комітетом. Пацієнти були розподілені на три групи: базова контрольна група з виключно неінвазивною візуалізацією, монодіагностична група з однією цільовою малоінвазивною інтервенцією та група комбінованого хірургічного дослідження.

Результати. Ізольоване радіологічне стадіювання супроводжувалося гіподіагностикою прихованого перитонеального карциноматозу на рівні 47,0 % та гіпердіагностикою реактивних змін у грудній клітці на рівні 18,2 %. Синергічна комбінація методів підвищила діагностичну точність до 96,4 % за специфічності 98,2 %. Частота післяопераційних ускладнень становила 6,3 %, при цьому життєво небезпечних станів зареєстровано не було. Впровадження алгоритму було пов'язане зі зміною стратегії лікування у 42,1 % пацієнтів, що дозволило провести точне рестадіювання. Результати аналізу виживаності (СВ = 0,64; 95% ВІ 0,43-0,96; $p = 0,032$) інтерпретуються як нескоригований асоціативний зв'язок і виступають у якості пошукової вторинної кінцевої точки.

Висновки. Рутинні неінвазивні методи візуалізації призводять до значної кількості хибних висновків. Застосування малоінвазивного хірургічного дослідження у відібраних пацієнтів дозволяє точно уточнити стадію захворювання та тісно пов'язане з модифікацією стратегії лікування.

Ключові слова: колоректальний рак; стадіювання; перитонеальний карциноматоз; діагностична лапароскопія; торакокопія; малоінвазивні діагностичні методики.