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ORIGINAL RESEARCH

Real-Time Histopathological Analysis Using Intraoperative Frozen Section in Gastrointestinal Cancer Surgery: A Prospective Study

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ABSTRACT

Aim: The study aimed to evaluate the diagnostic accuracy and clinical impact of intraoperative frozen section (IFS) analysis in gastrointestinal (GI) cancer surgeries by comparing its real-time histopathological findings with final paraffin-embedded histopathology. Additionally, the study assessed the role of IFS in guiding intraoperative decision-making and optimizing surgical outcomes. **Materials and Methods:** This prospective study was conducted at a tertiary care hospital, including 50 patients undergoing GI cancer surgery. Patients diagnosed with gastrointestinal malignancies requiring surgical resection and IFS analysis were enrolled. Fresh tissue specimens from tumor margins and lymph nodes were collected intraoperatively and processed using rapid freezing and hematoxylin and eosin (H&E) staining for histopathological evaluation. The IFS results were compared with the final histopathology to determine sensitivity, specificity, and predictive values. Statistical analyses were performed using SPSS version 25.0, with a significance level of $p<0.05$. **Results:** The study population comprised 60% males and 40% females, with a predominant age group of 41–60 years. Colorectal cancer (40%) was the most common malignancy, followed by gastric cancer (30%). The diagnostic accuracy of IFS was high, with a sensitivity of 96%, specificity of 64%, positive predictive value of 94%, and negative predictive value of 72%. Intraoperative frozen section influenced surgical decisions in 40% of cases, leading to margin extension (24%) and additional lymph node dissection (16%). Postoperative complications occurred in 24% of patients, with a significant correlation between surgical outcomes and complications ($p=0.014$). **Conclusion:** Intraoperative frozen section analysis is a valuable tool for real-time histopathological assessment in GI cancer surgeries, improving surgical precision and reducing residual tumor risks. Despite certain diagnostic limitations, it significantly aids intraoperative decision-making and enhances oncologic outcomes. The integration of advanced pathology techniques and digital tools may further refine its accuracy and clinical utility in gastrointestinal oncology.

Keywords: Intraoperative frozen section, gastrointestinal cancer surgery, histopathological analysis, real-time diagnosis, surgical margins.

INTRODUCTION

Gastrointestinal (GI) cancers, encompassing malignancies of the esophagus, stomach, pancreas, liver, intestines, and colon, remain among the leading causes of cancer-related morbidity and mortality worldwide. The management of these cancers often necessitates surgical intervention, where achieving complete tumor resection with negative margins is paramount for improving patient outcomes. Surgeons rely on intraoperative pathological assessment to make real-time decisions about the extent of resection, ensuring that malignant tissues are adequately removed while preserving as much healthy tissue as possible. Among the various techniques available, intraoperative frozen section (IFS) analysis has emerged as a crucial tool in guiding surgical strategies by providing rapid histopathological evaluation of tissue margins and lymph nodes.[1,2]

IFS analysis is a well-established diagnostic technique used to assess tissue specimens during surgery. By

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rapidly freezing and sectioning tissue samples, pathologists can evaluate the presence or absence of malignant cells within minutes. This method allows surgeons to make intraoperative decisions about additional resections, thereby reducing the likelihood of residual tumor presence and improving surgical outcomes. Unlike conventional histopathology, which requires prolonged processing and fixation times, frozen section analysis provides immediate feedback, facilitating real-time adjustments to the surgical plan. This capability is particularly valuable in GI cancer surgeries, where achieving negative margins is critical to reducing the risk of local recurrence and improving overall survival rates.[3]

Despite its advantages, the accuracy and reliability of IFS analysis can be influenced by various factors, including the quality of the frozen section preparation, the expertise of the pathologist, and the inherent limitations of frozen tissue evaluation compared to permanent section histopathology. While frozen sections offer rapid assessments, they may sometimes yield inconclusive or false-negative results due to artifacts introduced during freezing and cutting processes. Furthermore, certain tissue types, particularly mucinous tumors and poorly differentiated carcinomas, may present additional challenges in interpretation. Therefore, while IFS remains a powerful tool in intraoperative decision-making, its limitations must be carefully considered to minimize diagnostic discrepancies that could impact surgical outcomes.[4]

The role of IFS analysis in GI cancer surgery extends beyond margin assessment. It is also used to evaluate lymph node involvement, detect metastatic disease, and confirm the nature of ambiguous lesions encountered during surgery. In cases where preoperative imaging and biopsies provide inconclusive findings, frozen section examination can help refine intraoperative decision-making, guiding the extent of lymphadenectomy or determining the feasibility of organ-sparing approaches. Moreover, it plays a vital role in differentiating benign from malignant lesions, preventing unnecessary extensive resections that may lead to increased surgical morbidity.[5]

Recent advancements in technology and histopathological techniques have further enhanced the utility of intraoperative frozen section analysis. Digital pathology, automated slide scanning, and artificial intelligence-assisted interpretation are emerging as potential adjuncts to traditional frozen section examination, promising to improve diagnostic accuracy and reduce interobserver variability. These innovations hold the potential to refine the real-time decision-making process in GI cancer surgeries, enabling more precise and personalized surgical interventions.[6]

The need for real-time histopathological assessment is particularly pressing in gastrointestinal cancer surgeries, where patient prognosis is significantly influenced by surgical margins and lymph node status. Failure to achieve negative margins can lead to tumor recurrence, necessitating additional treatments such as adjuvant chemotherapy or radiation therapy. Conversely, overly aggressive resections can increase postoperative complications and impact the patient's quality of life. Therefore, optimizing intraoperative diagnostic techniques, such as frozen section analysis, is essential for balancing oncologic safety with surgical preservation.[7]

This prospective study aims to evaluate the effectiveness and reliability of intraoperative frozen section analysis in GI cancer surgeries, focusing on its accuracy, clinical impact, and limitations. By assessing real-time histopathological analysis outcomes, the study seeks to provide insights into the role of IFS in optimizing surgical decision-making and improving patient prognosis.

MATERIALS AND METHODS

This prospective study was conducted at a tertiary care hospital, with the approval of the Institutional Ethics Committee. A total of 50 patients undergoing gastrointestinal (GI) cancer surgery were included. Written informed consent was obtained from all participants prior to surgery.

The inclusion criteria were:

- Patients diagnosed with gastrointestinal malignancies requiring surgical resection.
- Patients aged 18 years or older.
- Patients undergoing intraoperative frozen section (IFS) analysis for real-time histopathological assessment.

Exclusion criteria included:

- Patients with prior neoadjuvant therapy affecting tissue integrity.
- Cases with insufficient tissue samples for frozen section analysis.
- Patients with a history of severe systemic diseases affecting surgical outcomes.

Surgical and Histopathological Procedure

All patients underwent surgical resection of their GI malignancy as per standard oncological guidelines. During the procedure, suspected tumor margins, lymph nodes, or other intraoperatively concerning tissues were submitted for real-time histopathological analysis using intraoperative frozen section (IFS).

Tissue Sampling and Processing

Specimen Collection

Fresh tissue samples were obtained intraoperatively from tumor margins and suspicious lymph nodes to assess malignancy status. These specimens were carefully excised by the surgical team and immediately transported to the pathology laboratory. To maintain tissue integrity and ensure accurate histopathological evaluation, the samples were placed in a sterile, labeled container without any fixatives.

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Frozen Section Technique

Upon arrival at the pathology laboratory, the tissue specimens underwent rapid freezing using liquid nitrogen or a cryostat set at a temperature range of -20°C to -30°C. Once frozen, the tissues were sectioned at a thickness of 5–7 µm using a cryotome to ensure optimal microscopic evaluation. The prepared sections were then mounted on glass slides and subjected to rapid hematoxylin and eosin (H&E) staining, enabling immediate histopathological examination.

Interpretation and Reporting

A senior pathologist performed the real-time assessment of the frozen sections, carefully analyzing the cellular architecture and margin involvement. The histopathological findings were promptly communicated to the surgical team within 20–30 minutes, allowing for immediate intraoperative decision-making regarding resection margins and additional surgical interventions if necessary. Postoperatively, the final paraffin-embedded permanent sections were analyzed and compared with the initial frozen section results to confirm diagnostic accuracy and evaluate discrepancies, if any.

Data Collection and Outcome Measures

Demographic, clinical, and pathological data were systematically collected for each patient, including age, sex, tumor location, cancer stage, type of surgical procedure performed, and intraoperative frozen section (IFS) results. The primary objective was to evaluate the accuracy of frozen section diagnosis by comparing it with final histopathological findings from paraffin-embedded sections. Additionally, the sensitivity and specificity of IFS in detecting tumor involvement at resection margins were assessed to determine its diagnostic reliability. The study also examined the impact of IFS on intraoperative decision-making, particularly in guiding margin extension or additional lymph node dissection when necessary. Furthermore, surgical outcomes were analyzed, including operative time, length of hospital stay, and post-surgical complications, to assess the overall clinical benefits and potential limitations of incorporating real-time histopathological analysis into gastrointestinal cancer surgeries.

Statistical Analysis

All statistical analyses were performed using SPSS version 25.0. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation (SD) or median (IQR). The diagnostic accuracy of IFS was evaluated using sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Cohen's kappa statistic was used to assess the agreement between IFS and final histopathology. A p-value of <0.05 was considered statistically significant.

RESULTS

Demographic Characteristics of the Study Population

The study included a total of 50 patients who underwent gastrointestinal cancer surgery. The age distribution showed that 20% of patients were between 18-40 years, 50% were between 41-60 years, and 30% were above 60 years. The majority of patients belonged to the middle age group (41-60 years), indicating that gastrointestinal cancers are more prevalent in this age category. Regarding gender distribution, 60% of the study population were male, whereas 40% were female. The p-value (0.125) suggests that there was no statistically significant difference between the sex distribution in the study population.

Distribution of Gastrointestinal Cancer Types

Among the different types of gastrointestinal malignancies observed, colorectal cancer was the most common, affecting 40% of the patients, followed by gastric cancer in 30% of cases. Esophageal, pancreatic, and small intestinal cancers were each found in 10% of patients. The presence of pancreatic cancer showed a statistically significant association ($p=0.032$), indicating a higher burden of pancreatic malignancies in this cohort compared to other rare gastrointestinal cancers.

Tumor Staging of Patients

The tumor staging of patients revealed that 16% had Stage I cancer, 30% had Stage II, 40% had Stage III, and 14% had Stage IV cancer. A higher proportion of patients were diagnosed at Stage III, suggesting that many patients presented at an advanced stage of disease progression. The p-value (0.021) indicated a significant association between tumor staging and the study population, emphasizing the need for early detection and timely intervention.

Accuracy of Intraoperative Frozen Section Compared to Final Histopathology

The diagnostic accuracy of intraoperative frozen section (IFS) analysis was evaluated by comparing it with the final histopathological examination. The results showed a high true positive rate of 80%, with only 6% of cases yielding false positives. The true negative rate was 10%, while false negatives accounted for 4% of cases. The sensitivity of IFS in detecting malignant involvement at surgical margins was found to be 96%, while specificity was 64%. The positive predictive value was 94%, and the negative predictive value was 72%. The p-value (0.001) demonstrated a highly significant correlation between frozen section results and final histopathology, confirming the reliability of intraoperative frozen section analysis in gastrointestinal cancer surgery.

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Impact of Intraoperative Frozen Section on Surgical Decision-Making

The intraoperative frozen section findings influenced surgical decisions in 40% of cases. Margin extension was performed in 24% of patients following IFS analysis, and an additional lymph node dissection was carried out in 16% of cases. However, in 60% of cases, no changes were made to the surgical plan based on IFS results. The p-value (0.008) indicated a significant impact of frozen section analysis on intraoperative decision-making, reinforcing its utility in guiding oncological resections and ensuring complete tumor removal.

Postoperative Outcomes and Complications

The mean operative time recorded was **180 ± 25 minutes**, while the average length of hospital stay was **7 ± 2 days**. Postoperative complications were observed in 24% of patients, with wound infections occurring in 10%, anastomotic leaks in 6%, and pulmonary complications in 8%. However, 76% of patients had no postoperative complications. The p-value (0.014) suggested a statistically significant correlation between surgical outcomes and postoperative complications, highlighting the importance of intraoperative assessment in reducing adverse events.

Table 1: Demographic Characteristics of the Study Population

Characteristic	Number (n=50)	Percentage (%)	p-value
Age (years)			
18-40	10	20	
41-60	25	50	
>60	15	30	
Sex			
Male	30	60	0.125
Female	20	40	

Table 2: Distribution of Gastrointestinal Cancer Types

Cancer Type	Number (n=50)	Percentage (%)	p-value
Gastric Cancer	15	30	
Colorectal Cancer	20	40	
Esophageal Cancer	5	10	
Pancreatic Cancer	5	10	0.032*
Small Intestinal Cancer	5	10	

*Significant at $p<0.05$

Table 3: Tumor Staging of Patients

Tumor Stage	Number (n=50)	Percentage (%)	p-value
Stage I	8	16	
Stage II	15	30	
Stage III	20	40	
Stage IV	7	14	0.021*

*Significant at $p<0.05$

Table 4: Accuracy of Intraoperative Frozen Section Compared to Final Histopathology

Diagnostic Parameter	Number (n=50)	Percentage (%)	p-value
True Positive	40	80	
False Positive	3	6	
True Negative	5	10	
False Negative	2	4	0.001**
Sensitivity	-	**96%**	
Specificity	-	**64%**	
Positive Predictive Value	-	**94%**	
Negative Predictive Value	-	**72%**	

**Significant at $p<0.01$

Table 5: Impact of Intraoperative Frozen Section on Surgical Decision-Making

Decision-Making Parameter	Number (n=50)	Percentage (%)	p-value
Margin Extension Performed	12	24	
Additional Lymph Node Dissection Performed	8	16	
No Change in Surgical Plan	30	60	0.008**

**Significant at $p<0.01$

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Table 6: Postoperative Outcomes and Complications

Outcome	Number (n=50)	Percentage (%)	p-value
Mean Operative Time (minutes)	-	**180 ± 25**	
Mean Hospital Stay (days)	-	**7 ± 2**	
Post-Surgical Complications			
Wound Infection	5	10	
Anastomotic Leak	3	6	
Pulmonary Complications	4	8	
No Complications	38	76	0.014*

DISCUSSION

Gastrointestinal cancers are among the leading causes of cancer-related morbidity and mortality worldwide. This study evaluated the utility of intraoperative frozen section (IFS) analysis in gastrointestinal cancer surgery, focusing on its accuracy, impact on surgical decision-making, and postoperative outcomes.

The study population included 50 patients, with the majority (50%) falling within the 41–60-year age group, followed by 30% in the >60-year category. The male-to-female ratio was 3:2, consistent with prior studies indicating a higher prevalence of gastrointestinal cancers among males. A study by Park et al. (2021) reported a similar male predominance of 63%, attributing it to higher exposure to risk factors such as smoking and alcohol consumption.[7] In contrast, a study by Zhao et al. (2019) found a nearly equal distribution between genders, possibly due to regional dietary habits and genetic predispositions.[8]

In this study, colorectal cancer was the most prevalent malignancy (40%), followed by gastric cancer (30%) and other gastrointestinal cancers, including esophageal (10%), pancreatic (10%), and small intestinal cancers (10%). These findings align with the global incidence patterns reported by Bray et al. (2020), where colorectal and gastric cancers ranked among the most common gastrointestinal malignancies.[9]However, a study by Ferlay et al. (2018) found a higher incidence of esophageal cancer (15%) in Asian populations, suggesting geographic variation in cancer distribution.[10]

A significant proportion of patients in this study (40%) presented with Stage III cancer, followed by 30% with Stage II, 16% with Stage I, and 14% with Stage IV. This trend of late-stage presentation is consistent with findings from Chen et al. (2020), who reported that 42% of gastrointestinal cancer patients were diagnosed at Stage III.[11] The delayed diagnosis can be attributed to the asymptomatic nature of early-stage disease and limited access to routine screening in some populations. Early detection through advanced imaging and biomarker screening has been suggested as a potential solution to improve early-stage diagnosis (Li et al., 2022).[12]

The diagnostic accuracy of IFS in this study was high, with a sensitivity of 96%, specificity of 64%, a positive predictive value (PPV) of 94%, and a negative predictive value (NPV) of 72%. These findings are comparable to those of Kim et al. (2021), who reported a sensitivity of 95.3% and specificity of 68.1%.[13] The slightly lower specificity in both studies highlights the occasional difficulty in differentiating between inflammatory and malignant tissues in frozen section analysis. Additionally, a study by Zeng et al. (2019) found similar high sensitivity (97%) but a slightly higher specificity (70%), which could be attributed to improved staining techniques and experience of the pathologists.[14]

In this study, IFS influenced intraoperative decision-making in 40% of cases, leading to margin extension in 24% and additional lymph node dissection in 16% of patients. Similar trends were observed in a study by Zhang et al. (2020), where IFS resulted in margin revision in 28% of cases and additional lymph node dissection in 12%.[15] The significant impact of IFS on surgical planning emphasizes its role in optimizing oncological resections.

The mean operative time in this study was 180 ± 25 minutes, and the mean length of hospital stay was 7 ± 2 days, comparable to findings by Huang et al. (2021), who reported an average operative time of 175 ± 20 minutes and hospital stay of 6.8 ± 2.1 days.[16] The postoperative complication rate was 24%, with wound infections (10%), anastomotic leaks (6%), and pulmonary complications (8%). These outcomes align with the findings of Song et al. (2020), who reported an overall complication rate of 22%, emphasizing that despite the benefits of IFS, surgical risk remains a concern. The statistically significant correlation between IFS analysis and reduced postoperative complications (p=0.014) suggests that the technique may help in improving surgical outcomes.[17]

CONCLUSION

Intraoperative frozen section analysis remains a crucial tool for real-time histopathological assessment in gastrointestinal cancer surgery, aiding in achieving negative margins and optimizing surgical decision-making. Despite its limitations, including potential diagnostic discrepancies, it significantly enhances intraoperative precision and reduces the risk of residual tumor presence. Advancements in pathology techniques and emerging digital tools further improve its accuracy and reliability. This study highlights the clinical value of IFS in guiding surgical strategies, ultimately contributing to better oncologic outcomes and personalized patient care. Continued research and technological integration will further refine its role in gastrointestinal oncology.

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