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Original Research Article

INTEGRATING MOLECULAR DIAGNOSTICS INTO STAGING LAPAROSCOPY FOR GASTRIC CANCER: CURRENT EVIDENCE AND FUTURE DIRECTIONS

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ABSTRACT

Background: To evaluate the current evidence and future directions for integrating molecular diagnostics into staging laparoscopy for gastric cancer.

Materials and Methods: This prospective study included 32 patients with biopsy-proven gastric carcinoma, assessing symptomatology, histopathological characteristics, and the prevalence of occult metastasis through clinical assessments and staging laparoscopy.

Results: The majority of patients presented with pain (68.75%), anorexia (59.37%), and weight loss (56.25%). Histopathology revealed a predominance of well-differentiated adenocarcinoma (43.8%). Occult metastasis was identified in 28.2% of patients, with liver and/or peritoneal metastasis constituting the majority of these cases.

Conclusion: While traditional clinical assessments remain foundational in gastric cancer diagnosis and staging, the integration of molecular diagnostics offers promising avenues for improving staging accuracy and personalized treatment planning. Overcoming the challenges of standardization and cost will be crucial for future advancements.

Keywords: Gastric cancer, Molecular diagnostics, Staging laparoscopy, Occult metastasis, Personalized medicine.

INTRODUCTION

Gastric cancer remains one of the most challenging malignancies to treat, with its prognosis heavily dependent on the stage at diagnosis. Traditional staging methods, including imaging and endoscopic assessments, have provided a framework for determining the extent of disease and guiding treatment decisions.[1] However, the integration of molecular diagnostics into clinical practice promises to revolutionize the approach to managing gastric cancer by offering a more nuanced understanding of tumor biology, heterogeneity, and metastatic potential.[2] This integration is particularly pertinent in the context of staging laparoscopy, a minimally invasive procedure that allows for direct visualization and assessment of the peritoneal and visceral surfaces for metastatic disease, which is a critical determinant of treatment strategy and prognosis in gastric cancer.[3]

Recent advancements in molecular diagnostics, including next-generation sequencing (NGS), liquid biopsies, and tumor biomarker analysis, have opened new avenues for personalized medicine in oncology, enabling the identification of genetic mutations, expression profiles, and other molecular alterations that can influence treatment response and survival outcomes.[4] These molecular insights can complement the macroscopic findings of staging laparoscopy, potentially enhancing the accuracy of staging, guiding therapeutic choices, and even identifying patients who may benefit from targeted therapies or enrollment in clinical trials.

The current evidence supporting the integration of molecular diagnostics into staging laparoscopy for gastric cancer is growing but remains in its nascent stages. Preliminary studies have demonstrated the

feasibility and potential benefits of this approach, including improved detection of micrometastases, prognostic stratification based on molecular profiles, and the identification of actionable molecular targets. However, several challenges persist, including the standardization of molecular diagnostic techniques, interpretation of complex molecular data in a clinical context, and the economic implications of widespread implementation.[5]

As we move forward, the integration of molecular diagnostics into staging laparoscopy for gastric cancer stands at the precipice of a new era in oncology. Future directions will likely focus on refining molecular diagnostic tools, expanding the evidence base through rigorous clinical trials, and developing interdisciplinary approaches that leverage the strengths of both molecular biology and surgical oncology.[6]

Ultimately, this integration aims to personalize and optimize the care of patients with gastric cancer, offering hope for improved outcomes in a disease that has long been associated with a dismal prognosis.

MATERIAL AND METHODS

1. **Study Setup and Design**

- **Study Area:** The study was conducted in the Department of Surgery at Indira Gandhi Medical College and Hospital, Shimla.
- **Study Duration:** The study spanned a period of one year.
- **Study Description:** This was a prospective study.

2. **Study Population**

- The study included patients with biopsy-proven gastric carcinoma in the Department of Surgery, IGMC, Shimla, who met the inclusion criteria.
- **Inclusion Criteria**

1. Patients with endoscopic biopsy-proven carcinoma of the stomach deemed resectable on CECT thorax, abdomen, and pelvis.
2. Those who provided consent to participate in the study.

- **Exclusion Criteria**

1. Patients who received neoadjuvant chemotherapy before staging laparoscopy.
2. Patients with proven metastasis on CECT thorax, abdomen, and pelvis.
3. Patients who did not provide consent.

3. **Methodology**

- All eligible patients underwent a series of investigations, including haemogram, renal function tests, liver function tests, CEA, CA 19-9, chest X-ray, CECT scan, staging laparoscopy, diagnostic lavage, and histopathological examination (HPE) of biopsy specimens obtained during staging laparoscopy.
- A written informed consent was obtained from all participants.
- Specific protocols were followed for CECT abdomen scan, staging laparoscopy, and diagnostic lavage.

4. **CT Protocol**

- CECT was performed on a 64-slice MDCT (Light Speed VCT Xte: GE Healthcare).
- Patients underwent an overnight fast and received approximately 1.5-2 liters of water as neutral oral gastrointestinal contrast, starting 2 hours prior to the scan.
- Dual-phase CECT was conducted in late arterial and portal venous phases.
- Scan parameters included a slice thickness and interval of 5mm and a helical scan type.
- Intravenous contrast dose was 1.5-2ml/kg body weight administered at a rate of 3.5–4 ml/second by an automatic pressure injector.

5. **Staging Laparoscopy Protocol**

- Patients were placed in the supine position under general anesthesia.
- A 12 mm sub/supra umbilical incision was made, and pneumoperitoneum with CO2 was established.
- Laparoscopy was performed using a 30° telescope, with additional 5-mm ports inserted as needed.
- The entire abdominal cavity was systematically inspected, and biopsies were taken from suspicious tissues.
- Peritoneal lavage was conducted in patients without occult metastases during diagnostic laparoscopy.
- Definitive surgery was performed on patients deemed resectable during laparoscopy.

6. **Diagnostic Lavage Protocol**

- The peritoneal cavity was washed with 200 ml of warm normal saline solution, instilled into different abdominal regions, and aspirated under direct vision.
- The aspirated fluid underwent centrifugation and staining using Giemsa and Papanicolaou methods.
- Experienced cytologists interpreted the results, classifying them as positive, negative, or suspicious based on cellular characteristics.

7. **Ethical Considerations**

- Written informed consent was obtained from all participants.
- Confidentiality of collected information was strictly maintained, and individual identities were protected.

Study results were intended solely for academic purposes and to frame recommendations for service improvement.

RESULTS

The study encompassed a cohort of 32 patients diagnosed with gastric cancer, aiming to delineate the symptomatology, histopathological

characteristics, and prevalence of occult metastasis. The findings are summarized across three pivotal aspects: clinical presentation, histopathological diversity, and the detection of occult metastasis.

Clinical Presentation: The analysis revealed that the most prevalent symptom among patients was pain, observed in 68.75% (n=22) of cases. This was closely followed by anorexia (59.37%, n=19), weight loss (56.25%, n=18), and vomiting (43.75%, n=14). Melena was the least common symptom, reported in 12.5% (n=4) of the patient cohort. In terms of physical signs, a palpable mass was identified in 81.2% (n=26) of patients, making it the most common clinical sign, whereas pallor was noted in 59.3% (n=19) of the cases.

Histopathological Findings: Histopathology of the tumors demonstrated a predominance of well-differentiated adenocarcinoma in 43.8% (n=14) of the patients. This was followed by poorly differentiated adenocarcinoma in 25% (n=8), moderately differentiated adenocarcinoma in 18.7% (n=6), signet ring adenocarcinoma in 6.3% (n=2), mucinous adenocarcinoma in 3.1% (n=1), and neuroendocrine carcinoma, also in 3.1% (n=1) of the cases.

Occult Metastasis Detection: The staging laparoscopy identified occult metastasis in 28.2% (n=9) of patients. Specifically, liver metastasis was found in 6.3% (n=2), peritoneal metastasis in 9.4% (n=3), and a combination of liver and peritoneal metastasis in 12.5% (n=4) of the patients. A majority, 71.8% (n=23), presented with no evidence of occult metastasis.

In summary, the results highlight the significant variability in clinical presentations and histopathological types among patients with gastric cancer. The occurrence of occult metastasis, as detected through staging laparoscopy, underscores the critical need for comprehensive diagnostic approaches to inform optimal therapeutic strategies.

Table 1: Distribution of Patients According to Signs and Symptoms

SYMPTOMATOLOGY	NO. OF PATIENTS	PERCENTAGE
SYMPTOMS		
PAIN	22	68.75
ANOREXIA	19	59.37
VOMITING	14	43.75
WEIGHT LOSS	18	56.25
MALENA	4	12.5
SIGNS		
PALLOR	19	59.3
PALPABLE MASS	26	81.2

Table 2: Distribution of Patients According to Histopathology

HISTOPATHOLOGY	NUMBER OF PATIENTS	PERCENTAGE
ADENOCARCINOMA WELL DIFFERENTIATED	14	43.8
ADENOCARCINOMA MODERATELY DIFFERENTIATED	6	18.7
ADENOCARCINOMA POORLY DIFFERENTIATED	8	25
SIGNET RING ADENOCARCINOMA	2	6.3
MUCINOUS ADENOCARCINOMA	1	3.1
NEUROENDOCRINE CARCINOMA	1	3.1

Table 3: Distribution of Patients According to Occult Metastasis

OCCULT METASTASIS	NO. OF PATIENTS	PERCENTAGE
LIVER METASTASIS	2	6.3%
PERITONEAL METASTASIS	3	9.4%
LIVER + PERITONEAL METASTASIS	4	12.5%
ABSENT	23	71.8%
TOTAL	32	100%

DISCUSSION

The integration of molecular diagnostics into staging laparoscopy for gastric cancer represents a promising advancement in the personalization of cancer care.[7] Our study underscores the critical role of traditional clinical assessments in diagnosing and staging gastric cancer, as evidenced by the symptomatology and histopathological findings in our patient cohort. The prevalence of pain, anorexia, weight loss, and the detection of palpable masses aligns with existing literature, emphasizing the aggressive nature of gastric cancer and its significant impact on patients' quality of life.[8]

The histopathological diversity observed, with a predominance of well-differentiated adenocarcinoma, underscores the heterogeneity of gastric cancer. This variability necessitates a more nuanced approach to treatment, wherein molecular diagnostics could play a pivotal role by enabling the

identification of specific molecular alterations that could inform targeted therapy options.[9]

The detection of occult metastasis in a notable fraction of our cohort highlights the limitations of conventional diagnostic tools and the potential value addition of molecular diagnostics. Molecular tools, such as circulating tumor DNA (ctDNA) analysis and next-generation sequencing, could offer more sensitive detection of micrometastases, thereby refining staging accuracy and guiding therapeutic decision-making more effectively.[10]

Despite these promising prospects, the integration of molecular diagnostics into clinical practice faces challenges, including the need for standardization, the interpretation of complex molecular data, and the economic implications of widespread implementation.[11] Addressing these challenges will require concerted efforts from researchers, clinicians, and policy-makers, alongside advancements in technology and bioinformatics.

CONCLUSION

Our study reinforces the pivotal role of traditional clinical assessments in the diagnosis and staging of gastric cancer while highlighting the potential benefits and current limitations of integrating molecular diagnostics into this process. Future research should focus on overcoming the technical and economic barriers to the integration of molecular diagnostics, with the ultimate goal of enhancing the precision and personalization of gastric cancer care.

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