Section: Pathology

Original Research Article

ROLE OF EXPRESSION OF P63 AND CALPONIN IN GASTROINTESTINAL TRACT CARCINOMAS

R. Kamaraj[1], K. R. Mohan[2], S. C. Sivaranjani[3], M. Johnraj Suresh[4]

[1]Senior Assistant Professor, Department of Pathology, Government Chengalpattu Medical College, Tamilnadu, India.
[2]Associate Professor, Department of Pathology, Government Vellore Medical College, Tamilnadu, India.
[3]Assistant Professor, Department of Pathology, Government Thoothukudi Medical College, Tamilnadu, India.
[4]Associate Professor, Department of Pathology, Government Thoothukudi Medical College, Tamilnadu, India.

Received : 02/01/2024
Received in revised form : 06/02/2024
Accepted : 22/02/2024

Keywords:
Gastrointestinal tract, Carcinomas, Diagnosis, Calponin.

Corresponding Author:
Dr. M. Johnraj Suresh,
Email: johnrajsuresh69@gmail.com.

DOI: 10.47009/jamp.2024.6.1.268

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (1); 1349-1353

Abstract

Background: Gastro intestinal malignancies produce major morbidity and mortality, totalling 27 % of all disease deaths globally, with the largest burden of 62 % in Asians. **Material and Methods:** A total of 60 cases of gastrointestinal tract carcinomas, 33 cases of GIT biopsies, and 27 cases of GIT specimens were taken for the study. The study was conducted for three years (from June 2014 to June 2017). H & E sections and immunohistochemistry were done for the blocks of formalin-fixed paraffin-embedded sections. In addition, IHC was done using p63 and calponin. **Results:** Among the sixty cases, most patients are men (40), while just 30% are women (18). Most patients are 61 – 70 years old, constituting 22 cases (35%). Adenocarcinoma was the most prevalent histological diagnosis, accounting for almost 88% of all cases. Positive results were found in 37 (61.7%) cases (strong) and 23 (weak) (38.3%). In 9 of these 17 cases, Calponin expression was very positive, whereas in 8 cases, it was only weakly positive. Staining for p63 and calponin showed a significant p-value of 0.0001. **Conclusion:** Patients with colorectal carcinomas were found to benefit from lower metastasis, angiogenesis, and invasion rates when calponin expression was elevated. Lymph node metastases and tumour grade were also correlated with high p63 expression.

INTRODUCTION

Cancer is a primary global cause of disease, death, and loss of ability. The geographical distribution of malignancies of the gastrointestinal tract is particularly intriguing compared to cancers of other organs. Cancers of the digestive tract (or gastrointestinal tract) are considered gastrointestinal malignancies. These cancers include but are not limited to gastric, colorectal, hepatocellular carcinoma, oesophagal, and pancreatic cancer. Overall, gastrointestinal malignancies constitute the leading cause of cancer-related mortality. The incidence and fatality rates of gastrointestinal cancer are rising worldwide, and Asia is no exception to this trend.[1]

Cancers of the digestive system account for around 27% of all tumours and 20% of all cancer deaths globally, with Asia bearing 62% overall. It is crucial to define the type with histological and immunohistochemical molecular genetic markers for prognostic relevance and target-based therapy, as GIT malignancies are rising in developing nations like India.[2] Approximately 50-60% of stomach adenocarcinomas are found in the pylorus and antrum, followed by 25% in the cardia and 15% in the body or fundus; these tumours can take several forms, including exophytic, flat, or ulcerated. Well-formed glands bordered by columnar to cuboidal epithelial cells characterise the intestinal type of GA. In contrast, individual or poorly formed nests of cells expanding in an infiltrating pattern represents the more diffuse type of GA (signet ring cell carcinoma). Evaluation of gastrointestinal carcinomas relies heavily on the results of immunohistochemistry studies. Promising results have been seen with the use of the different markers P63 but also calponin in gastrointestinal tract cancers.[3]

The diagnostic potential of p63's widespread overexpression in a particular cell and tissue types has led to its use in the field of pathology. p63 immunohistochemistry (IHC) is widely used to label basal cells in prostatic and mammary glands, which

ISSN (O): 2687-5365; ISSN (P): 2753-6556

play an essential role in cancer detection. Tumour type identification is a common clinical use for p63 in combination with other antibodies; for example, squamous cell carcinoma may be distinguished from the adenocarcinoma in lung samples or urothelial carcinoma from renal cell carcinoma in kidney malignancies.[4] Since the discovery of p63 antibodies, over two thousand studies have examined its expression by immunohistochemical staining (IHC) in a wide range of malignancies, yielding widely varying p63 favourable rates across a wide variety of tumour types. Oesophageal, stomach, colon, and anal squamous cell carcinomas and their prognoses can be assessed using the nuclear marker P63. Extreme positivity in more than half of tumour cells is associated with a dismal prognosis.[5]

Calponin is used as a cytoplasmic stain. The contractions of vascular smooth muscle cells have been shown in certain studies to prevent metastases from occurring when their expression is high in the blood arteries of colonic tumours. In the upcoming years, these two immunohistochemical markers will be used to help predict the diagnosis and management of gastrointestinal tract malignancies and will have a role in cancer immunotherapy.[6]

Aim

This study aims to examine the role of the expression of immunohistochemical markers P63 and calponin in the development of gastrointestinal tract malignancies.

MATERIALS AND METHODS

A Retrospective and prospective study were conducted at Govt Chengalpattu Medical College, Chengalpattu and GAAMCH & RI, Kaarapettai, duration of 3 years (June 2014-June 2017). Sixty cases of GIT carcinomas, 33 GIT biopsies, and 27 GIT tissues were used in the study.

Tissue blocks of patients diagnosed with gastrointestinal tract malignancies are included in the study. In addition, patients with non-carcinomatous gastrointestinal lesions, neuroendocrine tumours, and lymphomas, as well as those whose tissue blocks were obtained before undergoing radiotherapy or chemotherapy, are not eligible to participate in the study.

Hematoxylin and eosin staining of tissue sections, immunohistochemical staining for p63 and calponin, and pathological staging and grading of gastrointestinal adenocarcinomas comprise the histopathological examination.

Over half of tumour cells show positive staining for p63 protein, indicating that its expression is high. The prognosis is grim. Staining duration: one week (5% tumour cell positivity) improved prognosis.

Staining of blood vessels in stromal tumours as positive for calponin. Strong staining indicates a good prognosis, whereas weak staining indicates a bad one.

All the numbers have been examined. SPSS 20V was used to analyse the primary data entered into a Microsoft Excel spreadsheet. Frequency and percentage calculations were made for the statistical analysis. The Chi-square test, with a threshold of 5%, was used to examine the correlation between the categorical data.

RESULTS

Seventy percentage of the instances include male patients (42 out of 60 total), whereas 30% involve female patients (18). Most sufferers are 61 to 70 years old, representing 22 cases (35%). (35%). Two of the instances were discovered in people younger than 30. (3.4%). As much as 22% of all GI cancers begin in the stomach (antrum) (36.7%). Consisting of around 16 (26.7%). The least frequent location was the ileum (1.7%). [Table 1]

The most prevalent histological diagnosis was adenocarcinoma (88.5%), with just one case being of the intestinal type. Adenosquamous and malignant melanoma made up just 2 of the cases, making them the rarest (3.3% each).

The instances were separated into 20 of them (28.3%). As a result, it was determined that 22 cases had considerable differentiation (36.7%). On the other hand, poor differentiation was identified in 18 patients (33.3%). [Table 2]

Seventeen of the sixty patients had highly significant P0.001 staining for P63, all of which were poorly differentiated carcinomas. Well-differentiated carcinomas are typically poorly stained for P63. A total of 17 instances were positive for lymph nodes, with 12 cases displaying mild P63 staining (representing three positive nodes) and five cases displaying severe P63 staining (representing >3 positive nodes). In contrast, 8 of the nine patients who tested negative for lymph nodes had just minor P63 staining.

Thirty-seven (61.7%) showed strong positive, whereas 23 patients showed only weak staining (38.3%). Well-differentiated carcinomas stained strongly, while poorly differentiated carcinomas stained weakly.

Seventeen instances had positive lymph node status, whereas nine had negative lymph node condition. Calponin expression was positively detected in 9 of these 17 (strong staining) and negatively seen in 8 (poor staining) cases. With a p-value of less than 0.03, the latter group was very positive in all nine situations. For the combination of p63 and calponin staining, the p-value was 0.0001. [Table 3]

Table 1: Distribution of patient's characteristics

Variable		Frequency	Percentage
Gender	Male	42	70
	Female	18	30

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Age	≤30	2	3.4
	31-40	4	6.7
	41-50	8	13
	51-60	20	33.4
	61-70	21	35
	>70	5	8.5
Site	Oesophagus	2	3.3
	Colon	9	15
	Rectum	16	26.7
	Stomach	22	36.7
	Ileum	1	1.7
	Anus	10	16.7

Table 2: Histopathological diagnosis

Histopathological diagnosis		Frequency	Percent
Infiltrating adenocarcinoma	Conventional	47	78.4
	Mucinous	5	8.3
	Intestinal type	1	1.7
Malignant melanoma		2	3.3
Infiltrating squamous cell carcinoma		3	5.0
Adenosquamous carcinoma		2	3.3
Histopathological grade	Poorly differentiated	18	30.0
	Moderately differentiated	22	36.7
	Well-differentiated	20	33.3

Table 3: Characterisation of p63 and calponin staining patterns

P63		Weak staining	Intense staining	P-Value
Histopathological grading	Poor	1	17	0.001
	Moderate	20	2	
	Well	20	0	
Lymph node	NA	21	13	0.29
	Negative	8	1	
	Positive	5	12	
Calponin	Poor	18	0	0.001
	Moderate	4	18	
	Well	1	19	
Lymph node	NA	15	19	0.03
	Negative	0	9	
	Positive	8	9	
Calponin	Weak staining	6	17	0.0001
	Strong positive	35	2	

DISCUSSION

According to Baydar DE et al. studies, stomach cancer strikes people between 50 and 60, while large intestine cancer typically strikes people between 60 and 70. 2.46:1 is the male to female ratio, with stomach lesions being the most prevalent, accounting for almost 50% of all cases, and the oesophagus is the least common, accounting for 2.6% of all cases. Adenocarcinomas were the most common histological diagnosis, accounting for 91.67%. After GIST, non-Hodgkins lymphoma is the next most prevalent histological diagnosis.[7]

Bansal et al. found that gastrointestinal tract (GIT) lesions, including benign and malignant, accounted for 3.18% of patients they examined. Among all benign lesions, appendicitis accounted for 52.14 %. Most cancers of the digestive system are adenocarcinomas (48.57%). The second most frequent cancer is Squamous cell carcinoma (37.14%). Most oesophageal tumours were squamous cell carcinomas. However, adenocarcinomas are the most prominent lesion in the stomach and large intestine. The histopathological analysis is the gold standard for finding lesions in the gastrointestinal system. It is beneficial for spotting cancerous lesions so they may be treated as soon as possible.[8]

Studies were conducted by Parikh BJ et al. The median age was in the 60s, and the male-to-female ratio was 2.03 to 1. Among the several gastrointestinal (GI) organs, the colorectal area had the highest incidence of tumours (38.46%), led by the oesophagus (28.57%), the gastric (19.78%), the small intestine (9.89%). Malignant tumours accounted for 89.01%, and benign ones for 10.99%. The most prevalent malignant tumour type was adenocarcinoma (45.68%). Based on the conclusions, the morphology of gastrointestinal malignancies varies greatly. Therefore, a diagnosis cannot be made without undergoing a histological study.[9]

According to the study by Steurer S et al., the expression of p63 was detected in a wide range of normal tissues, which include squamous epithelium and urothelium. Among 115 distinct tumour forms, 61 (53%) were positive. Cancers of the thymus and squamous cells showed the most significant levels of p63 positive (96–100%). Aberrant p63 expression was associated with lymph node metastases in 4%

ISSN (O): 2687-5365; ISSN (P): 2753-6556

of 355 gastric tumours. The results show that p63 immunohistochemistry is a useful diagnostic tool since p63 expression is so common in certain tumours.[10]

A study by Albasri AM et al. found that the through of p63 was absent in normal mucosa but present in 12.5% of adenomas. There was a significant correlation between age and high p63 expression, which was seen in 24.1% of individuals. The Kaplan-Meier analysis showed that increased levels of p63 were associated with a decreased chance of survival. Over-expression of p63 was found to be an independent predictive factor in patients using the Cox regression model. The results indicate that cytoplasmic p63 expression plays a crucial role in tumour growth and prognosis.[11]

According to a study by Song Y et al., the percentage of gastric carcinomas with positive p63 expression was much greater than in normal gastric mucosa tissues. Lymph node metastasis, tumour depth of invasion, tumour size, and TNM stage were all substantially linked with P63 expression. Outcomes Patients with gastric cancer with high levels of p63 have a terrible prognosis.[12]

According to the study by Praveen K et al., only 6.11 % of GIT biopsies were taken from the oesophagus, 17.22 % from the stomach, 2.22 % from the GE junction, 37.22 % from the small intestine, and 37.22% from the large intestine. Results show that early malignant tumours can be detected using endoscopy and subsequent biopsy for diagnosis. Since the mucosa is not visible during an endoscopic biopsy, the extent of the invasion cannot be determined.[13]

Lee DW et al. studied 521 individuals with mucinous adenocarcinoma and AIM. They were more likely to have a proximal site and microsatellite instability but less likely to have an angiolymphatic invasion. These findings suggest that mucinous adenocarcinoma is associated with a worse prognosis for individuals with stage II or III colorectal cancer who undergo adjuvant FOLFOX treatment.[14]

In a study by Mahmoud K et al., 61.4% of the 604 incidences of primary gastrointestinal cancers were found in men and 38.6% in females. There was an average 58-year-old in the population. With 30.7% of male cases and 36.0% of females, pancreatic cancer was the most frequent malignancy overall. Eighty percent of the patients were above the age of forty, and the median age at which most of the tumours were diagnosed was over sixty.[15]

Lin L et al. conducted thirty cases with average age of 56 years, 56.7% female. Among the initial carcinomas linked to gastrointestinal metastases, breast cancer accounted for the highest percentage (11 patients, 36.7%), followed by lung cancer (4 patients, 13.3%) and stomach cancer (9 patients, 30%). Nine patients (30.0%) with adenocarcinoma and ductal carcinoma were the most common pathologies. 33.3% of patients received GI treatment at the local level. The findings suggest that invasive ductal carcinoma of the breast is the most common source of gastrointestinal metastases. Poor prognosis is expected if gastrointestinal metastases are presented alongside other common metastases, while surgery may help some patients.[16]

A comprehensive study by Schizas D et al. revealed a total of 47 articles reporting on collision cancers in the gastrointestinal tract. While 96.2% of tumours had at least two histologically different components, just two instances had three or more. Within the first 24 hours following surgery, three individuals had problems.[17]

CONCLUSION

High levels of calponin expression were shown to reduce tumour metastasis, angiogenesis, and invasion in patients with colorectal carcinomas. Furthermore, lymph node metastases and tumour grade positively correlate with elevated p63 expression.

REFERENCES

1. Ghadyalpatil NS, Supriya C, Prachi P, Ashwin D, Avanish S. Gastro-intestinal cancers in India: Treatment perspective. South Asian J Cancer. 2016;5(3):126–36.
2. Wong HH, Chu P. Immunohistochemical features of the gastrointestinal tract tumours. J Gastrointest Oncol. 2012;3(3):262–84.
3. Gatti V, Fierro C, Annicchiarico-Petruzzelli M, Melino G, Peschiaroli A. DeltaNp63 in squamous cell carcinoma: defining the oncogenic routes affecting the epigenetic landscape and tumour microenvironment. Mol Oncol. 2019;13(5):981–1001.
4. Bir F, Aksoy Altinboga A, Satiroglu Tufan NL, Kaya S, Baser S, Yaren A. Potential utility of p63 expression in the differential diagnosis of non-small-cell lung carcinoma and its effect on the prognosis of the disease. Med Sci Monit. 2014; 20:219–26.
5. Zhang C, Schmidt LA, Hatanaka K, Thomas D, Lagstein A, Myers JL. Evaluation of napsin A, TTF-1, p63, p40, and CK5/6 immunohistochemical stains in pulmonary neuroendocrine tumours. Am J Clin Pathol. 2014;142(3):320–4.
6. Stojsic J, Jovanic I, Markovic J, Gajic M. Contribution of immunohistochemistry in the differential diagnosis of non-small cell lung carcinomas on small biopsy samples. J Buon. 2013;18(1):176–87.
7. Baydar DE, Kulac I, Gurel B, De Marzo A. A case of prostatic adenocarcinoma with aberrant p63 expression: presentation with detailed immunohistochemical study and FISH analysis. Int J Surg Pathol. 2011;19(1):131–6.
8. Bansal, Nidhi; Roy Choudhury, Arnav K et al. A Histopathological Spectrum of Gastrointestinal Tract Lesions in a Tertiary Care Centre in South Western Part of India: An Epidemiological Study. J. Krishna Inst. Medical Sci. Univ. 2018;7(3):43-47.
9. Parikh BJ, Parikh SB. Histopathological spectrum of gastrointestinal tumours: Natl J Integr Res Med. 2016;7(2):14–7.
10. Steurer S, Riemann C, Büscheck F, Luebke AM, et al. P63 expression in human and normal tissues: A tissue microarray study on 10,200 tumours. Biomark Res. 2021;9(1):7.
11. Albasri AM, Elkablawy MA, Ansari IA, Alhujaily AS, et al. The prognostic significance of p63 cytoplasmic expression in colorectal cancer. An immunohistochemical study: An immunohistochemical study. Saudi Med J. 2019;40(5):432–9.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

12. Song Y, Liu D, He G. TKTL1 and p63 are biomarkers for the poor prognosis of gastric cancer patients. Cancer Biomark. 2015;15(5):591–7.
13. Praveen K, Begum F, Kumar KM. Study of histopathological types of gastrointestinal lesions by endoscopic biopsy. Int. Arch. Integr. Med. 2016; 3(11): 46-53.
14. Lee D-W, Han S-W, Lee HJ, Rhee Y-Y, et al. Prognostic implication of mucinous histology in colorectal cancer patients treated with adjuvant FOLFOX chemotherapy. Br J Cancer. 2013;108(10):1978–84.
15. Mahmoud K, Musaad A, Alawad A. Pattern of primary gastrointestinal tract cancer in a central tertiary hospital in Sudan: A prospective study. Open Sci. 2014;1(4):34-37.
16. Lin L, Wang X, Tang C, Liang J. Clinical characteristics and prognosis of gastrointestinal metastases in solid tumour patients: A retrospective study and review of the literature. Anal Cell Pathol (Amst). 2019; 2019:4508756.
17. Schizas D, Katsaros I, Michalinos A, Damaskos C, et al. Collision tumours of the gastrointestinal tract: A systematic review of the literature. Anticancer Res. 2018;38(11):6047–57.

ISSN (O): 2687-5365; ISSN (P): 2753-6556