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The role of B-catenin in esophageal adenocarcinoma

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2026, 43(6):807–810

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Ο ρόλος της Β-κατενίνης στο αδενοκαρκίνωμα του οισοφάγου

Περίληψη στο τέλος του άρθρου

OBJECTIVE **To elucidate the role of B-catenin, E-cadherin and the Wnt pathway as well as the expression levels of B-catenin and E-cadherin as potential biomarkers.** METHOD **The study was retrospectively collected by the archives of the First Laboratory of Pathology of the Medical School of the National and Kapodistrian University in Athens, Greece. Seventy-one (n=71) patients with esophageal adenocarcinoma were included in this two years study (2023–2025) in order to investigate the association between esophageal adenocarcinoma and B-catenin.** RESULTS **A total of 71 histopathologically confirmed cases of esophageal adenocarcinoma were examined. After investigating the expression of E-cadherin and B-catenin immunohistochemically, a moderate positive correlation was found between cytoplasmic B-catenin and tumor regression grade (TRG). A strong positive correlation was also found between the cytoplasmic and nuclear expression of B-catenin. Increased cytoplasmic expression is associated with increased nuclear expression of B-catenin, indicating activation of the Wnt pathway. Moreover, a positive correlation was found between E-cadherin expression and TRG. Higher was found the E-cadherin expression, better was the response to the treatment.** CONCLUSIONS **Concurrently targeting B-catenin and E-cadherin may offer therapeutic benefits in esophageal adenocarcinoma and could be used as prognostic biomarkers.**

Key words

Adenocarcinoma
B-catenin
E-cadherin
Esophagus
Wnt

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Esophageal cancer is considered as the ninth most common type of cancer and the sixth leading cause of cancer-related death worldwide.[1] Esophageal adenocarcinoma is associated with the aberrant expression of B-catenin and of the transmembrane protein E-cadherin. The role of B-catenin is important in intracellular signal transduction through the Wnt pathway, which plays a critical role in the development of esophageal cancer. Activation of the Wnt/B-catenin signaling pathway can be observed in many human cancers, including esophageal cancer.[2] B-catenin plays a central role as an adaptor protein, linking E-cadherin to the actin cytoskeleton, which is essential for maintaining cell adhesion. Furthermore, B-catenin remains a vital component of the Wnt signaling pathway, which influences various cellular processes, including gene expression and cellular behavior.[3] However, B-catenin and E-cadherin play an important role in cell adhesion and in the development and progression of adenocarcinoma.[4] Normally, B-catenin is linked to E-cadherin outside the cell membrane and maintains cell cohesion. More specifically, B-catenin is the principal regulator of the Wnt pathway. The Wnt signaling pathway is directly related to B-catenin and when activated, leads to the accumulation of B-catenin in the cell nucleus, to the transfer of oncogenes and at last to the development of aggressive tumors.[5]

Surgery, chemoradiotherapy, laser therapy, and electrocoagulation are the most important treatments of esophageal cancer.[6] The aim of this study was to examine the role of B-catenin, E-cadherin and the Wnt pathway, and the B-catenin and E-cadherin expression levels as potential biomarkers for the early detection or prognosis of esophageal adenocarcinoma.

MATERIAL AND METHOD

Patient characteristics

In this study, 71 (n=71) anonymous esophagogastre specimens were evaluated from patients diagnosed with esophageal adenocarcinoma, regardless of prior treatment history. Data was obtained between the years 2023 and 2025. The study population included adult male and female patients ranging from ages 47 to 94 years, with a median age of 67.08 years. There was a predominance of the male population, representing 83.1% (n=59) towards the females which represented the 16.9% (n=12) of the gender population. The clinicopathological characteristics of patients are shown in table 1.

Design

Data was derived by anonymous esophagogastre specimens obtained from patients diagnosed with esophageal adenocarcinoma. These specimens are derived from the First Laboratory of Pathology of the Medical School of the National and Kapodistrian University in Athens, Greece.

Statistical analysis

This study involved the analysis of biomedical data and employed statistical methods to investigate potential differences among selected parameters. As a retrospective study, formalin-fixed, paraffin-embedded (FFPE) tissue sections and correlational statistical techniques were applied to evaluate the expression of two types of immunohistochemical markers: B-catenin and E-cadherin. Statistical significance was set at a threshold of $p<0.05$. All analyses of the raw data were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 28.0.[7]

Table 1. Clinicopathological characteristics of patients.

Parameters	Mean	Scale
Age	67.08	47–94
	Number	**(%)**
Sex		
Male	59	83.1
Female	12	16.9
Location		
Gastroesophageal junction (GJ)	22	30.9
Non GJ	49	69.1
Surgical method		
Total gastrectomy	7	9.9
Partial gastrectomy	50	70.4
Ivory Lewis	10	14.1
Without	4	5.6
Histological subtype		
Mucinous adenocarcinoma	2	2.9
Ulcerative adenocarcinoma	38	53.5
No ulceration	31	43.6
Differentiation		
High	2	2.9
Medium	46	64.7
Low	23	32.4
Tumor Regression Grade (TRG)	31	
1	3	9.7
2	0	0
3	5	16.2
4	12	38.7
5	11	35.4
Stage T		
T_1	7	9.8
T_2	15	21.1
T_3	43	60.5
T_4	6	8.6
Lymph node infiltration (N)		
N_0	38	53.5
N_1	8	11.3
N_2	14	19.7
N_3	11	15.5

RESULTS

After the immunohistochemical study of the expression of E-cadherin and B-catenin/Wnt, there was found a very strong positive correlation between cytoplasmic and nuclear B-catenin ($r=0.956$, $p<0.001$): Increased cytoplasmic expression was associated with increased nuclear expression, indicating activation of the Wnt pathway (tab. 2).

It was also shown that there is a moderate negative correlation between the expression of nuclear B-catenin and TRG ($r=-0.389$, $p=0.031$). The higher expression of nuclear B-catenin was correlated with worse response to the treatment. This correlation is statistically significant. Furthermore, a positive correlation was found between E-cadherin expression and TRG ($r=0.304$, $p=0.034$). The higher E-cadherin expression was correlated with better response to the treatment. This correlation is also statistically significant (tab. 3).

DISCUSSION

Esophageal adenocarcinoma is related with the expression of nuclear and cytoplasmic B-catenin and of the

Table 2. Correlation between cytoplasmic and nuclear B-catenin.

			Cytoplasmic B-catenin %	Nuclear cytoplasmic B-catenin %
Spearman's rho	Cytoplasmic B-catenin %	Correlation coefficient	1.000	0.956**
		Sig. (2-tailed)	.	0.000
		n	71	71
	Nuclear B-catenin %	Correlation coefficient	0.956**	1.000
		Sig. (2-tailed)	0.000	.
		n	71	71

**Correlation is significant at the 0.01 level (two-tailed)

Table 3. Correlation between E-cadherin expression and Tumor Regression Grade (TRG).

		E-cadherin (%)	TRG
Spearman's rho	E-cadherin (%)		
	Correlation coefficient	1.000	0.304
	Sig. (2-tailed)	.	0.034*
	n	31	31
	TRG		
	Correlation coefficient	0.304	1.000
	Sig. (2-tailed)	0.034*	.
	n	31	31

*Correlation is significant at the 0.05 level (two-tailed)

transmembrane protein E-cadherin.[2] B-catenin is a critical mediator of intracellular signaling within the Wnt signaling pathway, and it plays a fundamental role in the initiation and progression of esophageal malignancies.[8] In this particular study of 71 patients with esophageal adenocarcinoma, a moderate positive correlation was observed between cytoplasmic B-catenin expression and TRG, indicating that higher cytoplasmic B-catenin levels were associated with improved tumor response to therapy. This correlation is statistically significant.[9] Furthermore, a very strong positive correlation was identified between cytoplasmic and nuclear B-catenin expression, suggesting that increased cytoplasmic expression was accompanied by increased nuclear expression with activation of the Wnt signaling pathway. In contrast, a moderate negative correlation was found between nuclear B-catenin expression and TRG, indicating that higher nuclear B-catenin levels were significantly associated with poorer tumor response to treatment.[10] A positive correlation was also observed between E-cadherin and tumor differentiation. Tumors with higher differentiation have higher levels of E-cadherin. However, this correlation was barely statistically significant. There was a moderate positive correlation between cytoplasmic B-catenin and TRG.[11] Higher expression was associated with better tumor response to treatment. The correlation was statistically significant. Nevertheless, the association of cytoplasmic B-catenin with age and sex was not statistically significant. However, there was a strong negative correlation between E-cadherin and nuclear B-catenin.[12] Loss of E-cadherin-mediated adhesion was associated with post nuclear translocation of B-catenin and activation of the Wnt pathway. Our findings imply that B-catenin and E-cadherin may be used as prognostic indicators for esophageal adenocarcinoma.

To conclude, the study indicated the role of the interaction between E-cadherin and B-catenin in the pathophysiology of esophageal adenocarcinoma. High E-cadherin expression is associated with better response to treatment and lower aggressiveness, while increased nuclear B-catenin is associated with activation of the Wnt pathway, with reduced response and increased aggressiveness. The evaluation of these markers may contribute to the prognosis and to the finding of treatment of esophageal adenocarcinoma.

ΠΕΡΙΛΗΨΗ

Ο ρόλος της Β-κατενίνης στο αδενοκαρκίνωμα του οισοφάγου

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ΣΚΟΠΟΣ Διευκρίνιση του ρόλου της Β-κατενίνης, της Ε-καντχερίνης και της οδού Wnt, καθώς και των επιπέδων έκφρασης της Β-κατενίνης και της Ε-καντχερίνης ως πιθανών βιοδεικτών στο αδενοκαρκίνωμα οισοφάγου. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Η μελέτη συλλέχθηκε αναδρομικά από τα αρχεία του Πρώτου Εργαστηρίου Παθολογικής Ανατομικής της Ιατρικής Σχολής του Εθνικού και Καποδιστριακού Πανεπιστημίου Αθηνών. Εβδομήντα ένας (n=71) ασθενείς με αδενοκαρκίνωμα οισοφάγου συμπεριλήφθηκαν σε αυτή τη διετή μελέτη (2023–2025) προκειμένου να διερευνηθεί η συσχέτιση μεταξύ του αδενοκαρκινώματος οισοφάγου και της Β-κατενίνης. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Εξετάστηκαν συνολικά 71 ιστοπαθολογικά επιβεβαιωμένες περιπτώσεις αδενοκαρκινώματος οισοφάγου. Μετά από ανοσοϊστοχημική διερεύνηση της έκφρασης της Ε-καντχερίνης και της Β-κατενίνης, διαπιστώθηκε μέτρια θετική συσχέτιση μεταξύ της κυτταροπλασματικής Β-κατενίνης και του βαθμού παλινδρόμησης όγκου (TRG). Διαπιστώθηκε επίσης ισχυρή θετική συσχέτιση μεταξύ της κυτταροπλασματικής και της πυρηνικής έκφρασης της Β-κατενίνης. Η αυξημένη κυτταροπλασματική έκφραση σχετίζεται με αυξημένη πυρηνική έκφραση της Β-κατενίνης, υποδεικνύοντας ενεργοποίηση της οδού Wnt. Επί πλέον, διαπιστώθηκε θετική συσχέτιση μεταξύ της έκφρασης της Ε-καντχερίνης και της TRG. Όσο υψηλότερη ήταν η έκφραση της Ε-καντχερίνης, τόσο καλύτερη ήταν η ανταπόκριση στη θεραπεία. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Η ταυτόχρονη στόχευση της Β-κατενίνης και της Ε-καντχερίνης μπορεί να προσφέρει θεραπευτικά οφέλη στο αδενοκαρκίνωμα οισοφάγου και θα μπορούσαν να χρησιμοποιηθούν ως προγνωστικοί βιοδείκτες.

Λέξεις ευρετηρίου: Αδενοκαρκίνωμα, Β-κατενίνη, Wnt, Ε-καντχερίνη, Οισοφάγος

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