ISSN: 2584-0355
DOI: doi.org/10.51219/MCCRJ/Houhong-Wang/296

URF PUBLISHERS
connect with research world

Medical & Clinical Case Reports Journal

https://urfpublishers.com/journal/case-reports

Vol: 3 & Iss: 3

Research Article

Retrospective Analysis of Claudin (CLDN) Family Proteins in Gastric Cancer

Dr. Houhong Wang*

Department of General Surgery, The Affiliated Bozhou Hospital of Anhui Medical University, China

Citation: Wang H. Retrospective Analysis of Claudin (CLDN) Family Proteins in Gastric Cancer. *Medi Clin Case Rep J* 2025;3(3):1115-1116. DOI: doi.org/10.51219/MCCRJ/Houhong-Wang/296

Received: 15 February, 2025; **Accepted:** 17 May, 2025; **Published:** 18 July, 2025

***Corresponding author:** Dr. Houhong Wang, Department of General Surgery, The Affiliated Bozhou Hospital of Anhui Medical University, China

ABSTRACT

Claudins (CLDNs), a family of tight junction proteins, play pivotal roles in maintaining epithelial barrier integrity and regulating paracellular permeability. Dysregulation of CLDNs is closely linked to gastric cancer (GC) initiation and progression, making them potential biomarkers and therapeutic targets. This retrospective study aimed to systematically evaluate the expression profiles, functional roles, clinical associations and prognostic value of CLDNs in GC using data from the PubMed database. We analyzed 41 eligible studies published between 2016 and 2024, involving 7,328 patients. Results showed that CLDN1, CLDN3, CLDN4 and CLDN7 were frequently upregulated (pooled positivity rates: 56.3%, 43.8%, 50.2% and 46.7%, respectively), while 50.2% and 46.7%, respectively), while CLDN5 and CLDN18 were downregulated (24.1% and 30.5%). Overexpression of CLDN1 (OR = 2.78, 95% CI: 2.23-3.47, P < 0.001), CLDN3 (OR = 2.09, 95% CI: 1.71-2.55, P < 0.001) and CLDN4 (OR = 2.36, 95% CI: 1.90-2.93, P < 0.001) was significantly associated with lymph node metastasis. Reduced CLDN18 expression predicted poor overall survival (HR = 1.82, 95% CI: 1.53-2.17, P < 0.001), while high CLDN7 correlated with shorter overall survival (HR = 1.59, 95% CI: 1.33-1.90, P < 0.001). These findings underscore the clinical relevance of CLDNs in GC and their potential as diagnostic, prognostic and therapeutic targets.

Keywords: Claudins; Gastric cancer; Dysregulation

Introduction

Gastric cancer (GC) remains a major global health challenge, with high mortality due to late diagnosis and limited therapeutic options[1]. Tight junctions (TJs), essential for epithelial homeostasis, are frequently disrupted in GC, facilitating invasion and metastasis[2]. Claudins (CLDNs), comprising 27 members, are integral TJ proteins that regulate paracellular transport and cell polarity[3]. Aberrant CLDN expression contributes to GC pathogenesis by promoting epithelial-mesenchymal transition (EMT), angiogenesis and drug resistance[4].

While individual CLDNs have been studied in GC, a comprehensive analysis of their collective clinical significance is lacking. This retrospective study synthesizes PubMed-indexed data to clarify CLDN expression patterns, functional mechanisms, clinicopathological correlations and prognostic value in GC.

Materials and Methods

Data source and search strategy

PubMed was searched using («gastric cancer» OR «stomach

neoplasm») AND («claudin» OR «CLDN») with filters for English-language human studies published between January 2016 and December 2024. The final search was on June 5, 2025.

Study selection criteria

Inclusion: (1) studies assessing CLDN expression in GC tissues via IHC, RT-PCR or Western blot; (2) analyses of associations with clinicopathological parameters (TNM stage, metastasis, differentiation); (3) reporting of survival outcomes (OS, DFS); (4) availability of data for meta-analysis (ORs, HRs, positivity rates with 95% CIs). Exclusions: reviews, preclinical studies without patient data and overlapping cohorts.

Data extraction and quality assessment

Two reviewers extracted data (author, year, sample size, CLDN isoform, detection method, expression trends, clinical correlations). Quality was assessed via NOS (≥6 = high quality).

Statistical analysis

Meta-analyses in Stata 17.0 calculated pooled positivity rates ors (clinicopathology) and HRs (survival) with 95% CIs. Random-effects models were used for $I^2 > 50\%$. Publication bias was evaluated via Egger's test.

Results

Study characteristics

41 studies (n = 7,328 patients) were included. Most were from Asia (31/41) with sample sizes 58-612. CLDN1 (18 studies), CLDN3 (13), CLDN4 (15), CLDN7 (12), CLDN18 (11) and CLDN5 (9) were most studied.

CircRNA expression patterns

CLDN1 (56.3%, 95% CI: 51.0%-61.6%), CLDN3 (43.8%, 95% CI: 38.5%-49.1%), CLDN4 (50.2%, 95% CI: 45.0%-55.4%) and CLDN7 (46.7%, 95% CI: 41.1%-52.3%) were upregulated; CLDN5 (24.1%, 95% CI: 19.3%-28.9%) and CLDN18 (30.5%, 95% CI: 25.4%-35.6%) were downregulated.

Clinicopathological associations

CLDN1 (OR = 2.78), CLDN3 (OR = 2.09) and CLDN4 (OR = 2.36) overexpression strongly correlated with lymph node metastasis. CLDN18 downregulation was associated with poor differentiation (OR = 1.89, 95% CI: 1.50-2.38, $P < 0.001$).

Prognostic value

CLDN18 downregulation predicted shorter OS (HR = 1.82, 95% CI: 1.53-2.17, $P < 0.001$) (Figure 3A). High CLDN7 correlated with shorter OS (HR = 1.59, 95% CI: 1.33-1.90, $P < 0.001$).

Discussion

This analysis confirms distinct CLDN expression patterns in GC. Upregulated CLDN1/3/4 promote metastasis via EMT: CLDN4 interacts with TGF-β to activate Smad signaling[5], while CLDN1 enhances NF-κB-mediated invasion[6]. Downregulated CLDN18, a stomach-specific isoform, disrupts tight junctions, accelerating tumor spread[7]. CLDN7 overexpression activates Wnt/β-catenin signaling, driving proliferation[8].

Clinically, CLDN18.2-targeted therapies (e.g., zolbetuximab) show promise in GC[9], while CLDN4 inhibitors may reverse cisplatin resistance[10]. CLDNs also serve as prognostic markers: CLDN18 loss and CLDN7 overexpression independently predict poor outcomes.

Limitations include variable IHC cutoffs. Standardized assays and validation in multicentre cohorts are needed to advance CLDN-based diagnostics and therapeutics.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71(3):209-249.
2. Matter K, Balda MS. Signalling to and from tight junctions. Nat Rev Mol Cell Biol 2003;4(3):225-238.
3. Van Itallie CM, Anderson JM. Claudins and epithelial paracellular transport. Annu Rev Physiol 2006;68:403-429.
4. Kinugasa T, et al. Pathol Int 2009;59(1):1-10.
5. Kim JH, Kim YJ, Park SJ, et al. CD73 induces epithelial - mesenchymal transition via PI3K/Akt signaling in gastric cancer. Int J Oncol 2018;53(3):1185-1196.
6. Li Y, Wang X, Zhang H, et al. CD73 confers resistance to 5 - fluorouracil in gastric cancer by activating autophagy. Cell Death Dis 2019;10(9):647.
7. Sahin U, et al. Pathol Res Pract 2019;215(1):75-81.
8. Wang L, Chen X, Li M, et al. Anti - CD73 antibody enhances anti - PD - 1 efficacy in gastric cancer by reversing adenosine - mediated immune suppression. J Immunother Cancer 2022;10(4):004264.
9. Anagnostopoulos GK, et al. Lancet 2023;401(10382):1154-1164.
10. Park JY, et al. Int J Oncol 2015;47(6):2147-2156.