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# Heterogeneity of COX-2 and multidrug resistance between primary tumors and regional lymph node metastases of gastric cancer

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ABSTRACT

**Aims and background.** Cyclooxygenase-2 (COX-2) is involved in the progression of gastric cancer; however, the role of COX-2 in multidrug resistance (MDR) is still unclear. This study aimed to elucidate the relationship between COX-2 and MDR so as to show the heterogeneity of gastric primary tumors and regional lymph node metastases.

**Methods.** Between 2008 and 2009, 56 primary tumor samples and paired metastatic lymph node tissues from gastric cancer patients confirmed by surgery and pathological examination in our hospital were collected. The expression levels of COX-2 and MDR-associated factors such as P-glycoprotein (P-gp), glutathione S-transferase pi (GST-π) and topoisomerase II alpha (Topo-II-α) were determined by immunohistochemical staining. Tumor cells from these tissues were cultured and the cell chemosensitivities for 11 chemotherapeutic agents were measured by sulforhodamine B assay.

**Results.** The expression levels of COX-2, P-gp and GST-π were significantly higher in metastatic lymph node tissues than in primary tumors, while the expression level of Topo-II-α was lower in metastatic lymph node tissues than in primary tumors (all $P < 0.05$). In primary tumors, COX-2 and GST-π were positively correlated and COX-2 and Topo-II-α were negatively correlated; in metastatic lymph node tissues, a positive correlation was found between COX-2 and P-gp (all $P < 0.05$). The inhibition rates of eADM, VP-16, THP and MMC on cells from primary tumors were significantly lower than those on cells from metastatic lymph nodes, while the inhibition rates of HCPT, L-OHP and VCR on cells from metastatic lymph nodes were lower than those on cells from primary tumors.

**Conclusion.** The expression of COX-2 and MDR-associated factors as well as cell chemosensitivities are different in primary tumors and regional lymph node metastases of gastric cancer, and this may be an indication of their heterogeneity.

***Key words:*** gastric cancer, regional metastatic lymph nodes, cyclooxygenase-2, multidrug resistance, chemosensitivity.

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