

Localized Gastric Cancer: Approaches in Japan

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Pattern of Metastasis in Gastric Cancer

The large data base of the National Cancer Center Hospital Tokyo shows that gastric cancer remains as local disease for a rather long period in its evolution, and control of lymph node metastasis is key to curing this disease.

Depth		No. pts	LN (%)	Liver (%)	Peritoneum (%)	5YSR (%)
pT1	M	1,063	3.3	0.0	0.0	93.3
	SM	881	17.4	0.1	0.0	88.9
pT2	MP	436	46.4	1.1	0.5	81.3
	SS	325	63.7	3.4	2.2	65.8
pT3	SE	1,232	78.9	6.3	17.8	35.5
pT4	SI	724	89.8	15.5	41.6	10.1
Overall		4,683	47.8	4.5	11.5	60.3

Abbreviations: M = mucosal, SM = submucosal, MP = muscularis propriae, SS = subserosal, SE = serosa invasive, SI = invasive to neighboring organs, LN = lymph node, 5YSR: 5-year survival rate.

Endoscopic Submucosal Dissection for Dysplasia and Early Invasive Cancer

For dysplasia, which usually does not have metastasis, the necessity of treatment is controversial. However, because lesions diagnosed as dysplasia often have submucosal invasion and/or lymph node metastasis, endoscopic submucosal dissection is now widely accepted for histologic confirmation of the invasive nature of the disease and metastatic potential – even in the West. This can be a precise diagnostic method and, at the same time, sufficient treatment for such lesions.

Standard Treatment for Resectable Locally Advanced Cancer

Although the Dutch and British Medical Research Council (MRC) randomized controlled trials (RCT) comparing D1 vs. D2 surgery failed to prove the efficacy of D2 lymphadenectomy, the Intergroup study (INT0116/SWOG9008) clearly showed that D1 surgery alone was not sufficient treatment and that local control by radiation added to adjuvant chemotherapy was effective for gastric cancer. At the same time, experienced surgeons in the West demonstrated results with D2 surgery in Western patients that were as good as those achieved in Japan; thus, local control through use of either D2 surgery or radiation is regarded as essential. In the East, a Taiwanese RCT demonstrated the benefit of D2 dissection over D1 for the first time. Although this is a small single-institution RCT, the results clearly demonstrate the benefit of D2 dissection for gastric cancer.

A large RCT to evaluate the role of super-extended lymphadenectomy showed no survival benefit of D3 dissection over D2. In the node-negative patients, however, D3 dissection showed large benefit, the reason for which is not yet known. At the current time, D2 dissection with experienced hands or D1 plus radiation are acceptable methods of local control.

A recent RCT evaluating the efficacy of postoperative adjuvant S-1 (TS-1) chemotherapy showed significantly better OS and relapse-free survival with S-1 than with D2 surgery alone. This is the first pivotal study to clearly demonstrate the benefit of adjuvant chemotherapy after D2 dissection.

Application of Neoadjuvant Chemotherapy

Although the MRC Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial of

perioperative chemotherapy showed significant improvement of survival in patients with gastric cancer, the results of both control and treatment groups were worse than in the INT0116 or Japan Clinical Oncology Group (JCOG) trials. Considering the burden to patients, costs, and prognosis of those who underwent D2 dissection, neoadjuvant treatment is focused on specific types of gastric cancer, such as linitis plastica or unresectable tumors with bulky nodal metastases. Some phase II studies of neoadjuvant treatment for such tumors have shown promising results.