Is there any role in adjuvant chemotherapy after curative resection for ICC?

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Surgical resection is the only way to cure biliary tract cancer. However, local recurrence or distant metastasis often occurs following curative resection and the prognosis in patients with recurrence is very poor. Five-year survival rates for cholangiocarcinoma are 10-40% overall and 30-52% following R0 resection in perihilar disease, 23-50% overall and 27-62% R0 in distal disease and 8-47% overall in intrahepatic disease. Therefore, further development of effective adjuvant therapy for preventing recurrence is eagerly anticipated.

The incidence of biliary tract cancer is low in Western countries, where a large number of clinical studies of adjuvant therapy have been conducted in other types of cancer. And few randomized clinical trials (RCTs) of postoperative therapy in bile duct cancer have been carried out. The only randomized study of adjuvant chemotherapy in bile duct caner was performed in Japan. In the study, 508 patients with pancreatic cancer and biliary tract cancer were assigned to a treatment group in which combination chemotherapy using 5-FU and mitomycin C was administered (MF group) and a surgery alone group. One hundred eighteen patients had bile duct cancer, 112 had gallbladder (GB) cancer, 158 had pancreatic cancer, and 48 had ampullary cancer. Five-year survival rate was significantly better in the MF group for GB cancer. However, the difference in survival rate was found only in patients with noncurative resection. On the basis of intent-to treat analysis, no significant difference between the MF and control group was observed in patients with GB cancer. And there is also no difference in bile duct cancer patients. An Italian study evaluated the benefit of adjuvant chemotherapy in intrahepatic cholangiocarcinoma. In this retrospective analysis, 575 patients treated with curative intent hepatectomy were recruited. After matching, no difference was observed between patients who had or had not adjuvant chemotherapy (n=155 per group; 3-yrs RFS 28.3% vs 38.0%, p=NS).

Recently, survival benefit of gemcitabine-based chemotherapy in nonresectable biliary tract cancer was proved in a large scaled randomized clinical trial. However, no large RCTs of postoperative adjuvant chemotherapy have been carried out with such regimens. RCTs of adjuvant therapy, using new agents such as gemcitabine and others, should be conducted and now a large scaled randomized clinical trial is ongoing in UK (UK BICAP study). In this study, a total of 360 resected biliary tract cancer patients will be randomized to receive either adjuvant chemotherapy with capecitabine or observation.

At the present time, no recommendable regimen as an adjuvant chemotherapy is available in biliary tract cancers including intrahepatic cholangiocarcinoma, so clinical trials of various types of adjuvant treatment should be carried out in the future.