Combined stenting and photodynamic therapy improves survival in late stage liver cancer patients

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A combined therapeutic approach of stenting and photodynamic therapy may improve survival rates for patients suffering from advanced liver bile duct cancer, according to a study published this month in *Clinical Gastroenterology and Hepatology*, the official journal of the American Gastroenterological Association (AGA) Institute.

Researchers in the study found that while stenting can help reinforce the bile duct to increase liver functionality, the light therapy assisted in attacking the cancer cells directly. The combined therapy led to significant reductions in mortality rates in the year following treatment, compared with stenting treatment alone.

“This is a very aggressive disease that we’re fighting, as most patients are diagnosed when we can only offer palliative care,” said Michel Kahaleh, MD, of the University of Virginia and lead investigator of the study. “What we found in this study is that combining therapies that fight the disease and help improve liver functionality can help extend the survival rates for these patients.”

In this study, 48 patients were treated for advanced cholangiocarcinoma over a five year period. Nineteen were treated with photodynamic therapy (PDT) and stents, while 29 patients were treated with biliary stents alone. In the group receiving combined therapy, the photodynamic agent (porfimer sodium, a commonly used agent) was injected and

activated, and plastic stents were inserted. PDT was repeated every three months, at which time all stents were replaced. If the team found blockages or shifting, stents were exchanged earlier to maintain optimal decompression.

The group treated with stenting and PDT showed improved survival rates compared to the stent-only group (16.2 months vs. 7.4 months). Mortality in the PDT group at three, six and 12 months was 0, 16 and 56 percent respectively, while the corresponding mortality in the stent group was 28, 52 and 82 percent respectively. The difference between the two groups was significant at three and six months, but not at 12 months. Upon further analysis, the team found that only the number of ERCP procedures and number of PDT sessions were significant in determining survival. In both groups, serum bilirubin was successfully reduced.

PDT is an evolving therapy that involves administering a photosensitizing agent and activating it using light illumination of a specific wavelength, which kills the targeted cells. PDT is thought to destroy cancer and neovascular cells and reduce tumor mass, and in earlier prospective trials, PDT was associated with a significant reduction in bilirubin (a red blood cell byproduct excreted in liver bile) and increased survival compared to historical data.

“While we are pleased with the results of the study, we need to better understand if the effect is attributable primarily to the photodynamic therapy or to the number of ERCP sessions,” said Dr. Kahaleh.

Adverse events specific to PDT included three patients with skin phototoxicity requiring topical therapy. Complications in the stent-only group included patients developing cholangitis after therapy with two patients dying as a consequence. Post ERCP pancreatitis was observed in four patients and duodenal perforation in one. Other adverse events in the stent group included a liver abscess (1), perforation (1) and non-St

elevation myocardial infarction, or heart attack (2). In the PDT group, seven patients (37 percent) developed cholangitis treated with antibiotics alone. No patients had contraindications to photodynamic therapy contrast agents, and all patients received prophylactic antibiotics prior to the procedures.

Analyses were performed to detect predictors of survival, including MELD score (Model for End-stage Liver Disease, the extent of the disease), age, treatment by chemotherapy or radiation, and number of ERCP procedures and PDT sessions. Successful therapy was defined by relief of cholangitis (infection caused by biliary blockage), jaundice and pruritis (itching) with a decrease of bilirubin to less than 75 percent of the pre-treatment value within 30 days.

Cholangiocarcinoma (cancer of the liver's bile ducts) is the second most common liver cancer and is associated with significant morbidity and mortality, diagnosed in about 2,000 new cases every year. The majority of patients (almost 80 percent) are diagnosed when surgery is no longer an option due to the extent of the disease, with most surviving up to three months without intervention or four to six months with decompression treatment, which helps maintain the function of the liver by opening the bile ducts.

Treatment for the disease has evolved from surgery to endoscopic management, which involves placing a plastic stent in the bile duct to manage flow and control the cancerous growth (ERCP). It has become a standard of care to manage jaundice and prevent cholestasis (blockage of the bile duct), with less morbidity and mortality than that associated with surgery. However, the efficacy of stenting is limited because they cannot independently attack the tumor cells.

Source: American Gastroenterological Association