Biliary Stenting Combined with Photodynamic Therapy

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Introduction

Cholangiocarcinomas arising from the common hepatic duct and the confluence of hepatic ducts, called Klatskin tumors (hilar cholangiocarcinoma), are slow growing adenocarcinomas with late metastases, presenting mainly as obstructive jaundice.

Although endoscopic biliary metal stenting is the mainstay of palliative treatment in patients with unresectable hilar CC, tumor ingrowth or overgrowth is a significant problem in uncovered stents. In particular, the duration of metal stent patency for hilar CCs was shorter than that for distal bile duct cancer because the malignant hilar stricture provides an acute angle that hinders full expansion of the metal stent and promotes biliary sludge formation within. Several clinical trials have reported the therapeutic effect of photodynamic therapy (PDT) for unresectable hilar CC. The ability of PDT to destroy cancer and neovascular cells may prolong stent patency. However, the effect of PDT on stent patency has not yet been determined. The efficacy of PDT on stent patency in unresectable hilar CC was reported in our center. This retrospective study show that the PDT prolonged the stent patency compared with metal stent alone.

The role of palliative endoscopic decompression of cholestasis

Hilar CC has an extremely poor prognosis, with an average five-year survival rate of 5%-10%. Surgery provides the only possibility for a cure, but due to its anatomical location and natural history, the disease is locally advanced in most patients at the time of diagnosis. Therefore, effective palliation to alleviate symptoms associated with jaundice and the prevention of biliary sepsis are the fundamental goals for most patients with hilar CC. Although relief of biliary obstruction by endoscopic placement of metal stents is regarded as an optimal palliative measure in hilar CC, the clinical course after even successful stent insertion is one of disease progression and death from liver failure or cholangitis within 4-9 months. This clinical course is related to the ability to decompress affected proximal segments and recurrent stent occlusion, because these stents are unable to remodel malignant tissues.
The effect of PDT for hilar cholangiocarcinoma

PDT is an evolving therapy for treatment of cancers that are resistant to standard oncologic treatment. PDT involves the injection of an intravenous photosensitizing drug followed by endoscopic application of light to the tumor bed. The interaction between light and the photoagent causes death of cancer cells and tumor thrombosis by generating oxygen free radicals. PDT is currently being used for cases of hilar cholangiocarcinoma.9,10 Even in patients with advanced hilar CC, PDT has been shown to improve survival, quality of life, and to have a performance superior to that of biliary stenting in uncontrolled and randomized controlled trials.3,11-13 In our study, Kaplan-Meier analysis demonstrated improved survival in the PDT group compared with the stent-only group (356 vs 230 d, \( P = 0.006 \)), in accordance with previous reports.8,11,13

Outcome of PDT with stenting

Effective palliation is essential, because biliary drainage and prevention of cholestasis are crucial for prevention of pruritus, cholangitis, and death in patients with hilar CC. The approach to palliative decompression has evolved from surgery and percutaneous to endoscopic management in order to prevent cholestasis and improve mortality. Endoscopy of hilar CCs is generally challenging and complex due to the involvement of multiple bile ducts requiring two or more stents; indeed, patency rates of endobiliary stents are lower than those of distal tumors.13,15,16 Moreover, the efficacy of endoscopic stenting in a hilar CC is often limited by stent patency, which is related to proximal tumor obstruction, because the stent does not affect tissue remodeling, unlike benign conditions.8,17,18 To address this issue, multiple studies have investigated the positive effects of the combination of bile duct stenting with PDT on patient survival.3,11,12 However, a paucity of information exists regarding the effect of PDT on stent patency.

In our study, metal stent patency was longer in the PDT group than in the stent-only group. The median stent patency was 215 d in the PDT group and 181 d in the control group (\( P = 0.002 \)). The main causes of obstruction of metal stents in bile ducts is tumor ingrowth or overgrowth.19 PDT offers the possibility of tumor ‘remodeling’, which can enhance or prolong the decompression effect.20 Accepting this hypothesis, the ability of PDT to destroy cancer cells and lessen cholestasis may prolong stent patency. In this context, this study is meaningful because the longer stent patency that is achieved by PDT may diminish the need for further procedures, such as stent revision or percutaneous biliary drainage, improving the quality of life of hilar CC patients whose prognosis is poor.

Conclusions

Metal stenting after one session of PDT may be safe with acceptable complication rates. The PDT group was associated with a significantly longer stent patency period and patient survival compared with the control group in patients with unresectable hilar CC. A prospective randomized multicenter study is required to confirm these data.

References

2. Quyn AJ, Ziyaie D, Polignano FM, Tait IS. Photodynamic therapy is associated with an improvement in survival in patients


