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Contents

Thrice Monthly Volume 12 Number 30 October 26, 2024

EDITORIAL

MINIREVIEWS

ORIGINAL ARTICLE

Retrospective Study

Clinical and Translational Research

World Journal of Clinical Cases

Thrice Monthly Volume 12 Number 30 October 26, 2024

Contents

LETTER TO THE EDITOR

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Contents

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LETTER TO THE EDITOR

Percutaneous transhepatic cholangiography: An effective option for endo-biliary radiofrequency ablation before stent insertion in unresectable biliary cancer?

Dimitrios S Karagiannakis

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Abstract

Biliary cancer is a highly aggressive disease that is typically diagnosed at advanced stages when surgical removal is no longer an option. In these cases, palliative care and mechanical widening of the blocked biliary system are preferred. The insertion of a stent is often necessary to prevent the recurrence of blockages caused by cancer progression. Prior to stent placement, endo-biliary radiofrequency ablation (EB-RFA) appears to result in longer-lasting stent effectiveness without increasing the risk of severe complications. However, its impact on overall survival is not yet clear. Additionally, while endoscopic retrograde cholangiopancreatography is the most common method for performing EB-RFA, percutaneous transhepatic cholangiodrainage seems to be a safe and potentially more efficient alternative, particularly for long, angulated, or significantly narrowed bile ducts.

Key Words: Biliary cancer; Cholangiocarcinoma; Pancreatic cancer; Percutaneous transhepatic cholangiodrainage; Radiofrequency ablation

Core Tip: Ablate or not prior to stent insertion in patients with unresectable biliary cancer? The role of endo-biliary radiofrequency ablation before stent remains unclear regarding the overall survival and the prolongation of stent patency. Contrary results are probably attributed to differences in the studies' design, cancer extensiveness, patient performance status, and applied technique. Moreover, it has to be clarified whether percutaneous transhepatic cholangiodrainage overcomes endoscopic retrograde cholangiopancreatography as the method of choice for performing ablation, especially in more complicated cases.

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TO THE EDITOR

Cholangiocarcinoma is the second most common type of liver cancer, following hepatocellular carcinoma, comprising 10%-15% of primary liver cancers in Western countries[1]. Extrahepatic cholangiocarcinoma, which includes perihilar cholangiocarcinoma (Klatskin tumor) and distal cholangiocarcinoma, makes up 80%-90% of cases, while intrahepatic cholangiocarcinoma accounts for the remaining 10%[2].

Pancreatic cancer is a leading cause of cancer death worldwide, with a dramatic increase in its prevalence over the last decades, which is expected to rise in the future[3].

Both these types of tumors have a high mortality rate due to their aggressiveness and the lack of easily noticeable clinical symptoms and specific diagnostic biomarkers, resulting in late diagnosis[4,5]. Hence, surgery, which is the best treatment option, is feasible for only a few patients, with the majority being treated with systematic therapy due to advanced, unresectable cancer[6]. Furthermore, many patients present extensive biliary obstruction, leading to jaundice, recurrent infections (cholangitis), increased morbidity, and poor quality of life. In this case, percutaneous transhepatic cholangiodrainage (PTCD) or endoscopic retrograde cholangiopancreatography (ERCP) are commonly used to control symptoms. At the same time, a biliary stent is often placed to keep the biliary tree open. However, stent patency may decrease over time with the aggravation of the untreated tumor[7].

RADIOFREQUENCY ABLATION THROUGH PTCD FOR ENDO-BILIARY CANCER

In the study published in the *World Journal of Clinical Cases*, Xing *et al*[8] evaluated the role of endo-biliary radiofrequency ablation (EB-RFA) under PTCD in these difficult-to-treat patients. The authors specifically investigated the efficacy and safety of this procedure regarding the post-operative stent patency time and complication rates such as bleeding and perforation[8]. Seventeen patients with unresectable biliary cancer were successfully treated with EB-RFA and stent placement through PTCD and followed every three months for nine months. Postoperative total bilirubin levels were significantly lower compared to the preoperative ones on the 7th postoperative day, and in only three patients, bilirubin values, though decreased, remained substantially higher than the upper normal limit, probably due to impaired liver function and not to biliary obstruction. Notably, the need for external drainage was eliminated on the 3rd to 5th postoperative day, the overall complication rate was acceptable, and adverse events when presented (2 episodes of bleeding and 1 of acute pancreatitis) were not life-threatening and easy to manage. Stent patency was 70% and 30% at three and six months, respectively, and the median survival time was four months[8].

There has been a debate about whether ablation before stent insertion decreases morbidity and improves survival compared to stent alone in patients with obstructive biliary cancer who are non-eligible for surgical treatment. In a retrospective study of 150 patients, Kong *et al*[9] recently showed no significant difference regarding survival between ablation plus stent and stent alone. However, the former group had a significantly higher duration of stent patency and a lower incidence of moderate bleeding and pain. Cui *et al*[10] retrospectively found technical and clinical success rates of 98% and 92%, respectively, in patients treated with EB-RFA and biliary stent placement for malignant biliary obstruction. The authors also indicated a median stent patency of 7 months and an overall survival of 5 months with no severe complications, such as bile duct perforation, bile leak, or acute pancreatitis in the post-procedure period, while only four patients required blood transfusion for post-procedure bleeding. Nevertheless, two patients died within 30 days after the EB-RFA procedure, both due to cholangitis and septic shock. These results agree with those presented by Xing *et al*[8].

However, on the other hand, Kang *et al*[11], in a prospective single-center randomized trial, did not demonstrate any significant difference between the EB-RFA/stent and the stent alone group regarding the 90-day stent patency rate, the median duration of stent patency, and the median overall survival (58.3% *vs* 45.8%; $P = 0.386$, 132 days *vs* 116 days; $P = 0.440$, and 244 days *vs* 180 days; $P = 0.281$, respectively). Importantly, the former group did not show procedure-related complications, such as bile duct perforation or hemobilia, while the early complication (< 7 days) rates did not differ between the two groups (4.2% *vs* 12.5%; $P = 0.609$). Similarly, Albers *et al*[12], in a randomized controlled (RCT) multicenter trial, including 44 patients treated with a self-expandable metal stent (SEMS) only and 42 patients treated with EB-RFA followed by SEMS insertion, did not show any significant difference concerning the 3-month and 6-month stent

patency between the two groups (81.8% *vs* 73.1% and 52.4% *vs* 33.3%; $P = 0.6$ for both respectively), whereas the addition of EB-RFA did not impact the survival (HR 0.72; $P = 0.389$). The two groups had not significantly different postoperative adverse event rates (2.3% *vs* 10.5%; $P = 0.18$).

Differences in the studies' design, cancer extensiveness, patient's performance status, and the applied technique (ERCP *vs* PTCD, stent's characteristics, time and intensity of EB-RFA, and number of EB-RFA sessions) are probably responsible for the disagreement among studies. A recent meta-analysis verified the importance of the study's design on the results. Comparing EB-RFA/stent versus stent alone concerning overall survival, the former was found to be superior [pooled mean increase in survival time 2.88 months (95%CI: 1.78-3.97), $I^2 = 77\%$, $P < 0.0001$]. When the RCTs ($n = 6$, 456 patients) were separately analyzed, the combination group provided a more prolonged overall survival as well [pooled mean increase in survival time 4.2 months (95%CI: 2.64-5.77), $I^2 = 23\%$, $P < 0.00001$]. Regarding the pooled mean stent patency time, the combination group showed a mean increase in stent patency time of 2.11 months (95%CI: 0.91-3.30, $I^2 = 84\%$, $P = 0.0005$) when the whole number of studies was included. However, when only RCTs were considered, the difference did not reach the statistical significance [pooled mean difference for stent patency time: 1.04 months (95%CI: −0.22 to 2.30), $I^2 = 55\%$, $P = 0.11$]. Concerning bleeding rates, abdominal pain, and episodes of cholangitis or pancreatitis, no significant differences were revealed between the two groups[13].

The study by Xing *et al*[8], published in the *World Journal of Clinical Cases*, does not answer whether or not to ablate. Its design (single-center, one-arm, retrospective study) and the small number of included patients make it incapable of fulfilling that role. However, it does emphasize the role of PTCD as an effective method for EB-RFA performance. While ERCP is the most common approach nowadays, PTCD appears to have a shorter operation time, a higher success rate, and a lower complication risk, and it is more effective than ERCP in overlong, angle-shaped, and extremely narrowed bile duct cases[14]. In some instances, cannulation failure, inaccessibility of the duodenum, and suboptimal positioning of the instrument due to pre-papillary obstruction and distortion may occur during an ERCP procedure. On the other hand, an essential advantage of PTCD is its effectiveness in addressing and ablating even perihilar or proximal hilum malignancies that are inaccessible by ERCP. This inaccessibility makes it difficult or infeasible for an RFA probe to establish direct contact with the cancer, which is necessary for a successful ablation[15].

A meta-analysis of 11 studies (1417 patients; 784 ERCP, 633 PTCD) recently showed a 3.5 times higher success rate of PTCD compared to ERCP, whereas ERCP was found to carry a 1.7-fold higher risk for cholangitis and 11.50 times higher risk for reintervention needing[16]. The study by Xing *et al*[8] demonstrated that EB-RFA could effectively be performed *via* PTCD, with 100% feasibility and 100% stent patency in the initial postoperative period, without increasing the risk of life-threatening complications.

CONCLUSION

Xing *et al*'s study brings to light the role of PTCD in managing patients with unresectable biliary cancer[8]. It is not intended as a standalone treatment but as an effective intercessor to EB-RFA performance. The study findings are noteworthy; however, they are constrained by their basis in a single-center and the small sample size. These limitations cast doubt on the interpretation and generalizability of the results. Therefore, validation is necessary by large, multi-center, 1:1:1 randomized controlled trials to compare the efficacy of EB-RFA/stent by PTCD or ERCP to stent alone. Such an approach is imperative for determining the most effective approach to managing symptoms and improving the quality of life in patients with unresectable biliary cancer while also minimizing the risk of severe complications.

FOOTNOTES

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