SYSTEMATIC REVIEW AND META-ANALYSIS

Radiofrequency ablation combined with biliary stent placement versus stent placement alone for malignant biliary strictures: a systematic review and meta-analysis

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Background and Aims: Unresectable malignant biliary strictures are generally managed by palliative stent placement for drainage of biliary tree. Recently, radiofrequency ablation (RFA) has been used to improve the patency of biliary stents in these patients. Several studies have evaluated the effectiveness of biliary stent placement with RFA on stent patency and patient survival with variable results. We performed this meta-analysis to evaluate the efficacy and safety of biliary stent placement with RFA compared with stent placement alone in patients with malignant biliary strictures.

Methods: We performed a comprehensive search of electronic databases for all studies comparing RFA with biliary stent placement versus stent placement only. Measured outcomes included patient survival, stent patency, and procedure-related adverse events. An inverse variance method was used to pool data on stent patency into a random-effects model. Cox-regression analysis was used to calculate hazard ratio for survival analysis. We used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework to interpret our findings.

Results: Nine studies (including 2 abstracts) with a total of 505 patients were included in the meta-analysis. The pooled weighted mean difference in stent patency was 50.6 days (95% confidence interval [CI], 32.83-68.48), favoring patients receiving RFA. Pooled survival analysis of the reconstructed Kaplan-Meier data showed improved survival in patients treated with RFA (hazard ratio, 1.395; 95% CI, 1.145-1.7; $P < .001$). However, RFA was associated with a higher risk of postprocedural abdominal pain (31% vs 20%, $P = .003$). Our analysis did not show significant difference between the RFA and stent placement–only groups with regard to the risk of cholangitis, acute cholecystitis, pancreatitis, and hemobilia.

Conclusions: In the light of this limited data based on observational studies, RFA was found to be safe and was associated with improved stent patency in patients with malignant biliary strictures. In addition, RFA may be associated with improved survival in these patients. (Gastrointest Endosc 2017;■:1-8.)

Malignant biliary tumors are commonly diagnosed at an advanced stage, and as a result most are unresectable. The primary goal of treatment in these patients is generally palliative, which includes therapies to relieve biliary obstruction. Biliary stent placement provides the least-invasive and cost-effective method of achieving biliary decompression.[1] Self-expanding metal stents (SEMSs) and plastic stents have been used to relieve biliary obstruction secondary to malignant tumors of biliary tract. Although the stent patency of SEMSs is superior to plastic stents, it is still limited to a median duration of 6 to 8 months.[2] Primary causes of stent occlusion include tumor ingrowth or epithelial hyperplasia in addition to biofilm deposition, biliary sludge, and formation of granulation tissue.[3]

Radiofrequency ablation (RFA) can safely induce tumor necrosis and is successfully used for the treatment of hepatocellular cancers.[4] Recently, intraductal RFA with an endobiliary catheter (Habib EndoHPB; EMcision, London, U.K.) has been used as an adjuvant therapy to potentially

Abbreviations: CI, confidence interval; RFA, radiofrequency ablation; SEMS, self-expanding metal stents.

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improve stent patency and survival. Several studies have evaluated the use of RFA in malignant biliary obstruction with conflicting results. The purpose of this meta-analysis was to compare the efficacy and safety of RFA and biliary stent placement versus stent placement alone in patients with malignant biliary obstruction.

METHODS

A computerized literature search was performed under the supervision of a University of Toledo librarian (W.L.). On March 30, 2017 search strategies and subsequent literature searches were performed by an experienced health sciences reference librarian (W.L.) in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[5] Search strategies that leveraged controlled vocabularies, keyword synonyms, and device brand names were developed for PubMed. This strategy was translated to be used in Embase, the Cochrane Central Register of Controlled Trials, and the Web of Science Core Collection databases on the Clarivate Analytics Web of Science platform. The searches accounted for plurals and variations in spelling with the use of appropriate wildcards.

The searches combined the following concepts: radiofrequency ablation with biliary stents. Within the results for those combined concepts, additional filters, publication types, and keyword strategies were used to identify and exclude the most common articles types that do not report trial results (reviews and case studies). An exhaustive forward search tool was used for Web of Science database to capture all possible studies of interest. The databases were searched for publications dates 2005 to present. No language limits were applied. Appendix 1 (available online at www.giejournal.org) details the exemplar PubMed search.

To identify further articles, references were handsearched. All results were downloaded into EndNote (Thompson ISI ResearchSoft, Philadelphia, Pa), a bibliographic database manager, and duplicate citations were identified and removed. In addition, abstracts from Digestive Disease Week, annual meetings of American College of Gastroenterology, and United European Gastroenterology Week from the last 5 years were also searched.

Inclusion criteria

Prospective and retrospective studies or abstracts were included that compared the clinical outcome, including patient survival and stent patency, after endoscopic biliary stent placement with or without RFA therapy. Adult human studies published in English were also included.

Exclusion criteria

Studies were excluded when information on the survival or stent patency in the patient groups with and without RFA was not provided. In addition, duplicate publications, animal studies, reviews, case reports, and letters were also excluded.

Assessment of study quality

Quality of studies included in the analysis was assessed by using the Newcastle-Ottawa Scale for cohort studies and the Cochrane tool for assessing the risk of bias for randomized control trials. The Newcastle-Ottawa Scale uses a tool that assesses quality in 3 parameters of selection, comparability, and exposure/outcome and allocates a maximum of 4, 2, and 3 points, respectively. High-quality studies are scored >7 on this scale and moderate-quality studies between 5 and 7. The Cochrane Collaboration has adopted the principles of the Grading of Recommendations, Assessment, Development and Evaluation system for evaluating the quality of evidence for outcomes reported in systematic reviews. We used the Grading of Recommendations, Assessment, Development and Evaluation framework to interpret our findings relevant to clinical practice.

Data extraction

Data were extracted by 2 authors (A.A.S. and M.A.K.) independently using characteristics of included studies. Parameters were study methodology, year of study, demographics, type of stent, etiology of malignant biliary obstruction, method of stent placement, RFA (endoscopic vs percutaneous), proportion of patients with distant metastasis, length of stricture, percentage of patients who received chemotherapy and radiation therapy, mean stent patency, mean survival, and adverse events in the 2 treatment groups. The kappa coefficient for agreement between the 2 reviewers was .77. In case of discrepancy between reviewers, agreement was reached by consensus after discussion with a third reviewer (A.D.).

Outcomes

The primary outcome of this study was to assess stent patency with the use of RFA in patients with malignant biliary obstruction. Secondary aims included assessing differences in overall survival and adverse events with the use of RFA. Corresponding authors of studies[6] were contacted if data on stent patency and survival were not reported. Authors who shared their data have been acknowledged.

Statistical analysis

The inverse variance method was used to pool data on stent patency into a random-effects model. Cochrane χ^2 and I^2 statistics were used to estimate statistical heterogeneity. Presence of heterogeneity was defined as $P < .1$ and $I^2 > 50\%$.

We expected heterogeneity in our estimate because studies had included patients with various etiologies of malignant biliary strictures and methods of attaining biliary drainage were not uniform (endoscopic and/or percutaneous). Therefore, predetermined subgroup analyses