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DOI: 10.17235/reed.2025.11257/2025

Link: [PubMed \(Epub ahead of print\)](#)

Please cite this article as:

Pérez Roldán Francisco, González Carro Pedro . Radiofrequency ablation for cholangiocarcinoma — Safety and effectiveness in clinical practice. Rev Esp Enferm Dig 2025. doi: 10.17235/reed.2025.11257/2025.

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## Radiofrequency ablation for cholangiocarcinoma — Safety and effectiveness in clinical practice

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*Authors' contribution: Writing-original draft: F. P. R.; writing-review and edition: P. G. C.*

*Conflicts of interest: F. P. R., and P. G. C. declare conflicts of interest with Boston Scientific (educational activities).*

*Artificial intelligence: The authors declare that they did not use artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.*

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Cholangiocarcinoma (CC) comprises a heterogeneous group of biliary tract neoplasms, and represents the second most common neoplasm of the liver (15 %) after hepatocellular carcinoma (1). Its incidence has increased over the past few decades and amounts to 3 % of all gastrointestinal cancers (2). According to anatomic location, specifically the Bismuth classification (2), these tumors are classified as intrahepatic, perihilar or distal CCs (20-30 %).

Only a minority of patients with CC have a known risk factor, usually sustained cholestasis, chronic bile-duct inflammation, or congenital abnormalities (2,3). Reported risk factors include age older than 65 years, smoking, obesity, diabetes, postsurgical bilioenteric anastomosis, chronic inflammatory conditions (primary sclerosing cholangitis, hepatolithiasis, liver cirrhosis, hepatitis B and C, HIV), parasitoses (*Opisthorchis viverini* and *Clonorchis sinensis*), congenital conditions (choledochal cysts, Caroli's disease and congenital hepatic fibrosis), chemicals (thorotrast, dioxin, nitrosamines and asbestos), and drugs (oral contraceptives and isoniazid).

The diagnosis is made using imaging techniques such as abdominal ultrasound, computed tomography, magnetic resonance imaging, and positron emission tomography. Cholangiography, whether by endoscopic retrograde cholangio-pancreatography (ERCP) or using the percutaneous transhepatic approach, is also useful (2,3). ERCP allows lesion sampling as well as placing stents to manage jaundice (2,3). Brush and bile aspiration cytology or biopsy collection under direct vision cholangioscopy are useful diagnostic methods (2,4). Also worthy of consideration is the utility of both endoscopic and intraductal ultrasound during ERCP, particularly in patients with a previous negative cytology result and to assess lymph node involvement.

The treatment of choice is surgical resection, including liver transplantation in selected cases, in association with capecitabine chemotherapy. However, diagnosis is usually delayed until an advanced, unresectable stage. In these cases chemotherapy with gemcitabine and cisplatin is recommended first-line, but response is poor. In the past few years immune therapy was introduced against several CC cell molecules as second-line treatment, with or without associated chemotherapy (3).

The role of radiation therapy in CC is still unclear but coadjuvant chemotherapy with radiation, has been recommended for intrahepatic and perihilar CC with positive margins and nodes, and also for unresectable perihilar CC ineligible for liver transplanty en el CC perihiliar irresecable no elegible para trasplante hepático (3).

For palliation in advanced or inoperable cases radiofrequency ablation (RFA) and transcatheter arterial chemoembolization may be attempted (2,3) to improve patient quality of life. Photodynamic therapy for unresectable extrahepatic CC seems to be a fine palliation option, perhaps even better than independent radiofrequency or stent use as single treatment (5).

Intraductal ablation by RF has proven to be safe, effective and feasible for the palliative treatment of extrahepatic CC, and a safe way of improving metallic stent patency (3,5). Two types of RF probes are currently available, both bipolar, which cause thermal injury to induce tumor tissue necrosis. These are the Habib™ EndoHBP (Boston Scientific) (6) and ELRA™ Endobiliary RFA treatment (Taewoong Medical) (7), their most obvious difference being their size and number of electrodes, as each has distinct power levels and application times.

Regarding results, Dolak et al. (8), in their study of 58 patients, showed that Habib RF is a safe technique for the palliative management of CC, with good outcomes in terms of both metallic stent patency and patient survival. In that study most patients had Klatskin tumors and in these various complications were reported, including 1 hepatic infarction, 7 cholangitides, 1 gallbladder empyema, and 3 hemobilia cases. In the series by Laquière A et al. (9) on 12 patients with Bismuth

I-IV CC no severe complications were reported.

Kadayifci A et al. (10) described the effectiveness of RF use on self-expandable metallic stents occluded by tissue growth within them (56 %) using the Habib catheter. It induces tissue necrosis and improves stent patency when compared to stent treatment alone (119 versus 65 days).

Kang H et al. (7) reported a series of 48 inoperable patients comparing the use or not of ELRA catheter RF and stent placement. While they found no differences between groups, there seemed to be higher stent patency rates and durations in patients undergoing RF, with hardly any complications. In the study by Lee YN et al. (11), who used ELRA only for extrahepatic CC, longer stent patency durations and higher survival rates were obtained.

The published and reported experience in Spain on the use of RF for CC or non-coated metallic stent recanalization in the biliary tract remains scarce. The experience of both Martí L et al. (12) with ELRA ELRA (Fig. 1A) and our team at Hospital Universitario La Mancha-Centro (13) with Habib (Figs. 1 B and C) is similar to that reported in the literature. Of note, the Habib catheter has the advantage that it may be used with the standard coagulation source available in many endoscopy units, such as the VIO 200-Erbe. In contrast, the ELRA catheter has its own energy source with temperature controls.

RF, as described above, is applied through a duodenoscope during ERCP. However, RF may also be applied during percutaneous transhepatic cholangiography (14,15). This technique is safe and cost-effective for the recanalization of biliary metallic stents occluded by the tumor. Kong YL et al. (15) compared the effectiveness and safety of RF application plus stenting versus using only metallic stents. They found that mean stent patency with RF is 11.2 months, with a mean survival of 12.3 months.

In summary, it may be said that biliary bipolar radiofrequency application during endoscopy is a safe, effective palliative technique that is indicated for inoperable CC with jaundice to recanalize the biliary tract as well as occluded metallic stents, and which may be even used before stent placement. Its indication is for hilar and particularly extrahepatic CC. Controlled studies should be carried out to better define its target tumor lesions and additional indications. It should likely be included in cholangiocarcinoma treatment protocols and in those for the recanalization of metallic stents occluded by other neoplastic tissues.

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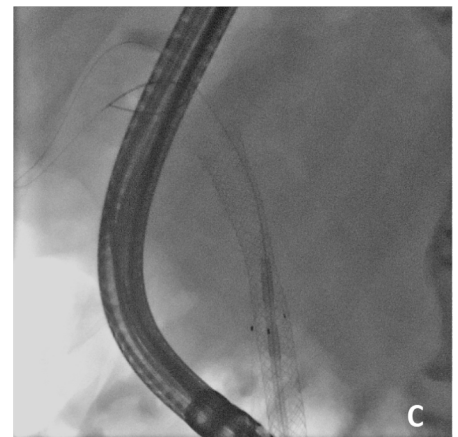
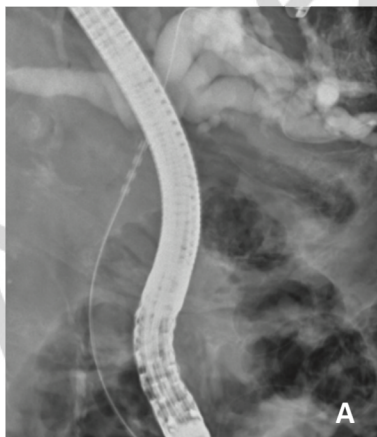




Fig. 1. A. ELRA catheter (courtesy of Dr. Martí). B. Habib™ EndoHBP probe (courtesy of Dr. Pérez Roldán). C. Habib™ EndoHBP probe for biliary stent recanalization (courtesy of Dr. González Carro).

Accepted Article