Adjunctive radiofrequency ablation for the endoscopic treatment of ampullary lesions with intraductal extension (with video)

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Background and study aims: Catheter-based radiofrequency ablation (RFA) delivered during endoscopic retrograde cholangiopancreatography (ERCP) may represent a viable treatment option for intraductal extension of ampullary neoplasms; however, clinical experience with this modality is limited. After ampullary resection, 4 patients with intraductal extension underwent adjunctive RFA of the distal bile duct. All patients received a temporary pancreatic stent to reduce the risk of pancreatitis, as well as a plastic biliary stent to prevent biliary obstruction. Three patients were treated for adenoma and 1 for adenoma with a focus of adenocarcinoma. During a short follow-up period, 3 patients experienced complete eradication of the target lesion, whereas the patient with a focus of adenocarcinoma had progression to overt invasive cancer. There were no immediate adverse events. One patient developed a post-RFA bile duct stricture, which has required additional endoscopic therapy. Catheter-based RFA of ampullary lesions that extend up the bile duct is technically feasible. Additional research is necessary to understand the risks and long-term benefits of this technique.

Introduction
Catheter-based radiofrequency ablation (RFA) delivered during endoscopic retrograde cholangiopancreatography (ERCP) has recently emerged as a possible therapeutic option within the bile duct [1–4]. Intraductal extension of neoplasm remains an important challenge in the endoscopic eradication of complex ampullary lesions [5,6], and RFA may represent a viable treatment adjunct for this problem. Recently, the use of RFA at the ampulla and within the distal bile duct has been described [7,8]. Herein we present 4 cases assessing the technical feasibility, safety, and treatment outcomes of RFA employed at the time of ERCP to treat ampullary lesions with intraductal extension.

Case Reports
The study was conducted at the Medical University of South Carolina (MUSC) from July 1, 2014 through October 1, 2015. After institutional review board approval, we retrospectively identified eligible adult subjects through the MUSC endoscopy report database (Endoworks, Olympus America, Center Valley, PA) by searching for reports that contained the keywords “radiofrequency ablation (RFA)” and “endoscopic retrograde cholangiopancreatography (ERCP)”. We excluded patients who underwent RFA of a stricture not associated with an ampullary lesion. We collected relevant clinical, histologic, and endoscopic data on all eligible subjects. All procedures were performed by an experienced pancreaticobiliary endoscopist under general anesthesia using a side-viewing duodenoscope. Included patients had undergone histologic evaluation of their ampulla prior to treatment. Ampullary resection was performed either en bloc or in piecemeal fashion by delivering electro surgical current through a snare with or without prior submucosal lift. Intraductal extension of the lesion was assessed cholangiographically (Fig. 1) and/or visually (Fig. 2). In some cases, a biliary sphincterotomy extension and papillary balloon dilation was performed to expose the inside of the terminal bile duct for assessment and therapy. Ablative therapy was delivered using a standard Argon Plasma Coagulation (APC) probe (ERBE USA Inc., Mariette, GA) at a flow rate of 1.0 L/min to 1.2 L/min and 30 to 40 maximum watts (W) and/or the Habib EndoHPB RFA bipolar cautery probe (EMcision United Kingdom, London, United Kingdom) at 10 W for 60 to 90 seconds, ex-
trapolating from manufacturer’s recommendations of 7 to 10W × 120 seconds [9]. Given the proximity to the pancreatic orifice and the benign nature of the target lesions, a shorter duration of treatment was chosen. In general, APC was reserved for treating exposed target tissue in the duodenum or very distal duct, whereas RFA was reserved for treating hidden or difficult to access tissue within the duct. All patients undergoing RFA received a temporary pancreatic stent (5Fr, 2–5 cm) and rectal indometacin to reduce the risk of post-ERCP pancreatitis (PEP), as well as a plastic endobiliary prostheses to prevent biliary obstruction and cholangitis.

Technical success was defined as the ability to successfully position the RFA probe across the biliary orifice and deliver thermal energy to the region of the papilla and terminal bile duct, resulting in coagulation of the visualized target areas. Clinical success was defined as endoscopic absence of polypoid or adenomatous-appearing tissue at the treatment site and histologic absence of neoplasm based on extensive follow-up biopsies from the papilla, pancreaticobiliary septum, biliary orifice, and distal bile duct. When the distal bile duct was not fully exposed by prior sphincterotomy, a pediatric biopsy forceps was introduced into the distal duct to acquire tissue. We intended to repeat RFA sessions until visual and histologic clearance was observed.

Patient demographics, procedure indications, and treatment outcomes are listed in Table 1. Four eligible patients were identified, all of whom were men with a mean age of 63 years (range 54–84). Three patients (75%) had a history of familial adenomatous polyposis (FAP). Three patients were treated for ampullary adenoma and 1 for ampullary adenoma with a focus of adenocarcinoma (he declined surgical evaluation).

Video 1 presents a synopsis of 2 representative cases. All RFA procedures were technically successful, resulting in a perceptible tissue effect (Fig. 3). RFA was performed immediately following endoscopic resection in 1 case and during a subsequent session in the remaining cases. The mean number of RFA sessions per patient was 1.5 (range 1–3). All patients were discharged uneventfully after the procedure without any immediate adverse events.

Table 1 Characteristics and outcomes of included cases.

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<tbody>
<tr>
<td>Age</td>
<td>54</td>
<td>84</td>
<td>54</td>
<td>58</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>FAP</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Histology</td>
<td>Adenoma</td>
<td>Adenoma with HGD/IMC</td>
<td>Adenoma</td>
<td>Adenoma</td>
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<tr>
<td>Sphincterotomy</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ampullectomy</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>APC sessions</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>RFA sessions, mean sec (range)</td>
<td>1, 80</td>
<td>3, 80 (70–90)</td>
<td>1, 75</td>
<td>1, 80</td>
</tr>
<tr>
<td>Follow up, days</td>
<td>56</td>
<td>105</td>
<td>38</td>
<td>51</td>
</tr>
<tr>
<td>Complications</td>
<td>No</td>
<td>No</td>
<td>Bile duct stricture</td>
<td>No</td>
</tr>
<tr>
<td>Treatment success</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Recurrence</td>
<td>No</td>
<td>Developed cancer</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

FAP, familial adenomatous polyposis; LGD, low-grade dysplasia; HGD, high-grade dysplasia; IMC, intramucosal cancer; APC, argon plasma coagulation; RFA, radiofrequency ablation; PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis; EUS, endoscopic ultrasound
ment seems reasonable. If the pancreatic and biliary orifices are
in close proximity, especially if adenoma appears to involve the
pancreaticobiliary septum, it may be best to perform the RFA ad-

djacent to a guidewire which has already been placed in the
pancreatic duct (subsequently guaranteeing pancreatic access for
stent placement) rather than adjacent to a plastic pancreatic
stant which may be damaged or even fractured during RFA.

Another safety concern is the development of clinically impor-
tant post-RFA biliary strictures that occurred in 1 of our patients,
akin to what has been observed in the esophagus after RFA of
Barrett’s epithelium [13]. This concern is particularly relevant in
the context of benign ampullary disease in which patients do not
typically undergo long-term stent placement, as is the case when
RFA is performed for palliation of malignant strictures. Along
these lines, until additional data are available, we have attempted
to minimize RFA across the cystic duct takeoff to avoid thermal
injury-related obstruction of the cystic duct, which has inten-
tionally been induced by electrohydraulic lithotripsy to treat re-
fractory bile leak [14].

In our series, RFA appears to have provided effective adjunctive
therapy in all 4 cases of benign pathology but was ineffective in
the setting of early adenocarcinoma, underscoring the concept
that surgical resection remains first-line therapy for ampullary
cancer (our patient declined surgery and chemoradiation). De-
spite the apparent effectiveness for benign lesions, it is important
to consider that intrabiliary extension is often nodular in nature,
leading to heterogeneous contact between the RFA probe and the
target tissue; this may lead to incomplete therapy and/or an in-
creased risk of buried neoplasm as is the concern when RFA is
used to treat nodular Barrett’s esophagus. Moreover, it can be
technically challenging to ensure circumferential contact of the
probe and the target tissue within a dilated bile duct, even when
luminal air is suctioned to induce collapse of the duct around the
probe. In these cases, a balloon-based RFA device that flattens
nodular tissue and maximizes treatment contact may be of value.

An additional consideration is that the proximal extent of neo-
plasm is often difficult to assess cholangiographically and the
role of cholangioscopy to guide probe placement should be fur-
ther explored. Prospective studies are necessary to evaluate these
issues and determine the long-term effectiveness of this modal-
ity.

In summary, catheter-based RFA after endoscopic resection of
ampullary lesions that extend up the bile duct is technically fea-
sible. Concerns regarding injury to the pancreas and bile duct as
well as incomplete treatment of nodular target tissue exist and
will be addressed by additional clinical experience and research.

Competing interests: None

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