Dear all,

With this newsletter we want to provide you with a summary of the latest developments in the research field of Early Neoplasia within the esophagus. Several topics within Barrett's Esophagus research and Early Squamous Neoplasia research will be addressed.

Barrett's Esophagus Research

Randomized trials

Recently a randomized trial, comparing safety of stepwise radical endoscopic resection (SRER) vs. focal ER followed by RFA, was published by van Vilsteren et al (Gut. 2011 Jan 5. [Epub ahead of print]) Patients with BE < 5 cm containing high-grade intraepithelial neoplasia (HGIN) or early cancer were included. Complete remission of neoplasia (CR-neo) was achieved in 25/25 SRER and in 21/22 (96%) ER/RFA patients. Complete remission of Intestinal Metaplasia (CR-IM) was achieved in 23 (92%) SRER and 21 (96%) ER/RFA patients. The rate of stenosis was significantly higher in SRER patients, 88% vs 14% (p <0.001), resulting in more therapeutic sessions in the SRER group. In conclusion: SRER vs. ER/RFA achieved comparable high rates of CR-neo/IM, however SRER was associated with a higher number of complications and therapeutic interventions. Therefore, in these patients ER/RFA may thus be preferred over SRER.

RFA in Long Segment Barrett's Esophagus

Thus far, RFA had only been assessed in short segment Barrett's Esophagus (<10cm). A recently published study by Herrero et al (Gastrointest Endosc. 2011 Apr;73(4):682-90.) assessed the safety and efficacy of RFA in BE ≥ 10 cm containing neoplasia. 26 patients were included, RFA treatment was preceded by ER in 18 cases. The worst residual histology pre-RFA treatment was HGIN (16 patients) and LGIN (10 patients). CR-neo and CR-IM were achieved in 83% and 79% respectively. None of the patients had fatal or severe complications, in 15% moderate complications were observed. Therefore it was concluded that ER followed by RFA is safe and effective in patients with BE ≥ 10 cm containing neoplasia, with a low chance of recurrence of neoplasia or BE during follow-up (29 months).

Durability of RFA treatment

Recently, Fleischer et al reported on the 5-year outcomes of the AIM-II trial (Endoscopy. 2010 Oct;42(10):781-9.) The AIM-II Trial included patients with nondysplastic Barrett's esophagus (NDBE) treated with radiofrequency ablation (RFA). At 5-year follow-up 50 out of 60 eligible patients consented for participation. In the majority of patients (92%) CR-IM was demonstrated. All failures (4 patients, 5/6 positive specimens obtained <1 cm of the squamocolumnar junction) were converted to CR-IM with a single focal ablation session. In this study, biopsy depth was found adequate to detect recurrence.

Quality of life (QoL) after RFA treatment

The impact of the diagnosis and treatment for dysplastic BE was poorly understood thus far. Therefore Shaheen et al assessed the influence of dysplastic BE on QoL and investigated whether RFA treatment would improve QoL in these patients (Endoscopy. 2010 Oct;42(10):790-9.) QoL of patients included in the AIM dysplasia trial (N Engl J Med. 2009 May 28;360(22):2277-88.) was assessed at baseline and at 12-months, by using a 10-item questionnaire specifically designed for this purpose. 127 patients in total were randomized to RFA (n=84) or sham treatment (n=43). Compared to the sham group, patients in the RFA arm had significantly less worry about esophageal cancer (p 0.003) and esophagectomy (p 0.009) after treatment. Other QoL related factors such as depression, impact on daily QoL, stress, general worry about the condition of the esophagus, etc. were also significantly reduced in the RFA arm after treatment. Therefore inclusion in the treatment arm was associated with improvement in disease-specific health-related QoL. This improvement appeared secondary to a perceived decrease in the risk for cancer.

Biopsy depth and the Buried glands Issue

In 2009 Pouw et al reported on the properties of the Neosquamous Epithelium (NSE) after RFA treatment (Am J Gastroenterol. 2009 Jun;104(6):1366-73.) The NSE was evaluated for genetic abnormalities and buried glandular mucosa. Patients who underwent RFA for BE containing HGIN or Early Cancer were analyzed. Sampling of the NSE was done by brush cytology, keyhole biopsies and endoscopic resection. Specifically, biopsy depth was compared in biopsies from NSE vs. untreated squamous epithelium. Presence of buried glandular mucosa was assessed in biopsies and the endoscopic resection specimen. Post-treatment NSE showed neither persistent genetic abnormalities nor buried glandular mucosa. Biopsy depth was similar in both treated and untreated epithelium and therefore deemed adequate for detection of buried glands.

In addition, in 2010 Shaheen and the AIM Dysplasia Investigators investigated biopsy depth after RFA of dysplastic BE (Gastrointest Endosc. 2010 Sep;72(3):490-496.e1) Depth of biopsy samples and prevalence of subepithelial structures after RFA treatment were compared to those of untreated controls. Almost 80% of all biopsy samples were adequate to evaluate for subsquamous intestinal metaplasia, as in both squamous and columnar tissue biopsy samples after RFA were as likely to demonstrate subepithelial structures as untreated controls. Biopsy sampling therefore appears to be of adequate depth to assess response to RFA therapy.

Early Squamous Neoplasia research

RFA for esophageal squamous HGIN and ESCC
Clinical evidence on the efficacy of RFA for early squamous neoplasia is limited. Recently, initial experiences in two tertiary centers, with RFA for squamous HGIN and esophageal squamous cell cancer (ESCC), were published by van Vilsteren et al (Endoscopy. 2011 Apr;43(4):282-90.) 13 patients (10 HGIN, 3 ESCC limited to the mucosa) with at least one unstained lesion (USL) were included. Following ER in 9 patients, median extent of USLs was 4cm and 50% of circumference. Complete response was achieved after a median of 2 RFA sessions, without recurrence during 17 month follow-up. Three stenoses were observed, treated with dilation. The results suggest that RFA in these patients is feasible and effective.

Endnote

On the RFA-academia website you can find the presentation Results of RFA which aims to give a summary of research on RFA over the past years. Finally we want to remind you that any interesting case reports can be submitted via the RFA-academia website, under the tab ‘Case discussions’.

On behalf of the RFA Academia steering committee,
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