UNIVERSITÄT
BERN

Medical Faculty
Institute of Pathology

Bern, August 4, 2015 dhe/alu

Tumor Budding in pT1 Colorectal Cancer: A retrospective international multicentric study

Background:

Submucosally invasive (pT1) colorectal cancer (CRC) is generally associated with low rates of nodal metastases, a subset of which can be managed by polypectomy or endoscopic mucosal resection alone. Identification of patients at risk for nodal metastases rests mainly on the recognition of adverse pathological features, such as lymphovascular invasion and high tumor grade. Many studies have also identified tumor budding as a risk factor for nodal metastases[1]. However, tumor budding is only rarely reported in pT1 CRC and is generally not considered a mandatory reporting category by major pathology and gastroenterology societies. One reason for this is that precise, reproducible and validated techniques are required in order for tumor budding to be safely used to influence patient management.

Aim:

The aim of this retrospective, multicentric study is to examine the role of tumor budding as a predictor of nodal metastases using the hotspot pancytokeratin method, which has shown promising results in terms of accuracy and interobserver variability[2].

Patient cohort:

As several centers have expressed interest in participating in this study, the exact number of patients remains to be determined. The study will encompass two patient groups, namely (A) patients having undergone primary local tumor resection (endomucosal resection or polypectomy) with subsequent segmental resection or patients initially having undergone segmental resection or (B) patients treated by local tumor resection alone (without subsequent lymph node resection).

Inclusion criteria:

pT1 cancers with the following information (to be filled out by participants via protocol)

- Date of birth, gender, anatomical subsite
- Histological subtype (WHO 2010), tumor grade (WHO 2010), presence/absence of venous invasion or lymphatic invasion
- Depth of tumor invasion (mm), Haggitt level (pedunculated lesions) or Kikuchi level (flat lesions)
- Distance from resection margin (mm)
- Klintrup score[3]
- **Group A:** Nodal status, **Group B:** Clinical follow-up (disease-free survival). This should be at least 3 years (36 months). Thus, the most recent case from Group B should not be more recent than August

2012. Group B patients with piecemeal/fragmented resection should have documented complete excision on follow-up endoscopy.

Exclusion criteria:

Patients with a history of:

- IBD
- Prior CRC/synchronous second CRC
- Polyposis syndrome (Lynch syndrome only if first CRC)

Participants will be required to:

- Fill out the protocol
- Send H&E stained slides and paraffin block(s) of resected specimen (polypectomy or initial segmental resection)

Methods:

Tumor budding will be assessed on pancytokeratin stained slides according to the 'hot-spot' (1HPF) method. The HPF in the densest area of tumor budding in the entire invasive tumor (overall tumor budding) and the HPF in the densest area of tumor budding at the invasive tumor front (peritumoral budding) will be assessed. Interobserver variability among several pathologists will be performed in a subset of cases.

Next step?

Interested participants please contact:

Heather Dawson, MD
heather.dawson@pathology.unibe.ch
Staff Pathologist
Institute of Pathology
University of Bern
Murtenstrasse 31
CH-3010 Bern, Switzerland
Phone: +41 31 632 9960

References:

1. Bosch SL, Teerenstra S, de Wilt JH, Cunningham C, Nagtegaal ID. Predicting lymph node metastasis in pt1 colorectal cancer: A systematic review of risk factors providing rationale for therapy decisions. *Endoscopy* 2013;**45**;827-834.
2. Koelzer VH, Zlobec I, Berger MD *et al.* Tumor budding in colorectal cancer revisited: Results of a multicenter interobserver study. *Virchows Archiv : an international journal of pathology* 2015;**466**;485-493.
3. Klintrup K, Makinen JM, Kauppila S *et al.* Inflammation and prognosis in colorectal cancer. *European journal of cancer* 2005;**41**;2645-2654.