

Overview on Colorectal papers

August 2002

A ProctoSite's e-publication

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Colorectal Cancer

April / May / June 2002

We have selected for this 'Overview' a list of 131 papers extracted from a total number of 520 retrieved from PubMed search over the last three-month for the keywords 'colorectal cancer'. As usual in ProctoSite's Selected Abstracts, colorectal cancer subjects are classified according five different subgroups:

1. Molecular biology

This is by far the most frequent subject of research and general publication in colorectal cancer in present time. Selecting those papers with potential interest for colorectal surgeons has been often a difficult task due to the wide range of aspects of molecular biology and genetics involved in many different studies. We have chosen fifty papers for this month selection according a rough criteria of potential clinical application.

Many genes candidates for markers

Molecular biology cancer studies are essentially undertaken by choosing genes and/or their respective protein products and assessing their functional status or action on tumour biological behaviour. Results from these studies may vary according the technique used and the frequent combined assessment of several markers in the same study is another important drawback for a clear understanding of its potential clinical application. An interesting illustration of the complexity of molecular biology analysis of colorectal cancer may be observed in the list below where we have compiled all markers included *only in the present selection of papers*:

- *Dihydropyrimidine dehydrogenase messenger RNA*
- *hMLH1 and hMSH2*
- *Androgen receptor status*
- *APC, K-ras, p53*
- *Matrix metalloproteinase-2 and -9*
- *Carcinoembryonic antigen*
- *H-cadherin*
- *Microsatellite instability*
- *Granulocyte-colony stimulating factor (G-CSF)*

- *TGF beta (1)*
- *T-cell costimulatory molecule OX-40 (CD134)*
- *Cyclooxygenase-2 (COX-2)*
- *Thymidylate synthase*
- *Vascular endothelial growth factor (VEGF)*
- *Thymidine phosphorilase*
- *erbB family*
- *Beta-catenin*
- *Intercellular adhesion molecule-1*
- *CA 50, CA 242*
- *Nuclear matrix proteins*
- *Nitric oxide*
- *Apoptosis index*
- *Ki-67*

This extensive but still partial list of genes / proteins under research demonstrates how difficult is to define the whole genomic tumour profile in colorectal cancer particularly considering that many of those markers have shown to act as independent prognostic factors in different carcinogenic steps such as cell proliferation, angiogenesis, adhesion or invasion. It has been also demonstrated that many of these markers play a different role in cell environment when studied alone or interacting with other markers. Thus, even though many of these markers have shown a significant recurrence or survival correlation, it seems unlikely that a single protein may fulfill the expected role of the "universal prognostic marker" in colorectal cancer prognosis

"In-block" gene studies: DNA microarrays

A possible way to deal with such a wide range of variables may be observed in two papers, published by [Stremmel and cols](#) and [Lin and cols](#) who emphasize the potential role of DNA microarrays to analyze thousands of genes in a single tissue sample in one experiment and to predict the biological behavior of colorectal cancer cells. These studies demonstrate that in-block gene assessment, rather than searching for an unique tumour marker, is possibly the shortest way to putting molecular biology in clinical practice.

Molecular diagnosis of cancer in stools

This non-invasive stool-based assay to identify colorectal cancer by molecular biology techniques have been used by [Davies and cols](#) and [Koshiji and cols](#). This is certainly an exciting new approach for early detection of colorectal cancer and deserves further evaluation.

Microsatellite instability (MSI)

We have included in this selection five studies about different aspects of microsatellite instability (MSI) in colorectal cancer. This hallmark of defective DNA mismatch repair (MMR) may be possibly considered as the most important prognostic factor since Dukes' lymphonodes studies in 1930. MSI-positive colorectal cancers present with typical phenotype and are associated with prolonged survival compared with

tumours that are microsatellite stable (MSS). Very interesting findings are reported by [Farrington and cols](#) , [Tsai and cols](#) , [Kondo and cols](#) , [Planck and cols](#) and [Jass and cols](#) .

Angiogenesis

This is a particular aspect of molecular biology of cancer which has received an increasing attention from many research centers. It has been strongly suggested an association between poor prognosis and increased microvascular density produced by tumour neoangiogenesis. We have included in this overview six papers about different aspects of angiogenesis which may help to understand present status of this issue. They were published by [Xiong and cols](#), [Nakasaki and cols](#), [Tokunaga and cols](#), [Karayiannakis and cols](#) and [Giatromanolaki and cols](#). These strong evidences for a critical role of angiogenesis in colorectal cancer have led to the development of strategies to achieve an extended suppression of the angiogenic process. An interesting paper about this subject has been included in the present overview published by [Shi and cols](#), who used gene therapy to express an inhibitor of endostatin which led to a sustained serum endostatin level sufficient to inhibit tumor cell-induced angiogenesis and to suppress both the initiation and subsequent growth of a human colorectal cancer model.

These above mentioned papers demonstrate how important is angiogenesis and we may possibly expect in a near future some real advances in the treatment of colorectal cancer.

2. Staging, follow-up and screening

This is another very frequent subject of studies regarding colorectal cancer and thirty-seven papers were included in this selection. Some related topics are highlighted here:

The role of colonoscopy or flexible sigmoidoscopy in colorectal cancer screening or follow-up programs

Five papers in the present list aim to investigate this still controversial issue and were published by the following authors: [Avidan and cols](#), [Syrigos and cols](#), [Imperiale and cols](#), [Zheng and cols](#), [Platell and cols](#).

Fecal occult blood screening

Another report from one of the most experienced groups in this very relevant subject may be found in this review, published by [Scholefield and cols](#).

Colorectal cancer risk factors

Some interesting epidemiological studies have been undertaken to detect the possible relationship between some supposed colorectal cancer related factors such as meat consumption and cigarette smoking ([Tiemersma and cols](#), [Terry and cols](#)), ingestion of fruits and vegetables ([Smith-Warner and cols](#)), general lifestyle factors ([Almendingen](#)

[and cols](#)), coffee and tea consumption ([Woolcott and cols](#)), use of anti-ulcer drugs ([La Vecchia and cols](#)), race ([Wudel and cols](#)) or sunlight exposure ([Freedman and cols](#)).

Other studies

Other colorectal cancer related studies are also included in this review about different subjects:

- Endoscopic ultrasound ([Kalantzis and cols](#), [Marusch and cols](#))
- Organization of a screening population program ([Bretthauer and cols](#))
- Quality of life in long term survivors ([Ramsey and cols](#))
- Investigations of asymptomatic liver metastasis ([Glover and cols](#))
- Colorectal cancer familiar story ([Mc Grath and cols](#), [Johns and cols](#))
- Chemoprevention with coxibs ([Rex and cols](#))
- Cost-effectiveness of treatment ([Van den Hout and cols](#))
- Metachronic colorectal cancer ([Evans and cols](#))
- Impact of intensive follow-up ([Renehan and cols](#))

3. Surgical treatment

Thirty-three studies related to surgical treatment were included. Results from surgical treatment in different series were reported by [Marusch and cols](#), [Helfritzsch and cols](#), [Wichmann and cols](#), [Chang and cols](#), [Isbister and cols](#), [Easson and cols](#).

Margins and surgeons

[Phang and cols](#) published a paper about the effects of positive resection margins and tumor distance in rectal cancer treatment outcomes. The variation of circumferential margin resection among surgeons and their respective results were reviewed by [Abbott and cols](#).

Prognostic significance of nodal disease and pathological determinants

[Rinkus and cols](#) have studied the significance of nodal disease following pre-operative radiotherapy. A large scale trial was undertaken by [Prandi and cols](#) to assess the prognostic role of lymphadenectomy in stage B colon cancer. Identification of pathological prognostic determinants was studied by [Petersen and cols](#) and [Nagtegaal and cols](#). A review about the feasibility of sentinel lymph node biopsy in colorectal cancer by [Fitzgerald and cols](#) was also included in present list of papers.

Laparoscopic resection in colorectal cancer

[Lujan and cols](#) present the five-year survival results of a series of laparoscopic resection for colon cancer. A prospective comparative study of laparoscopic versus open surgery for colorectal carcinoma with a mean follow-up of five years was reported by [Champault and cols](#).

Other studies

- Pre-operative anemia as risk factor for colon cancer ([Dunne and cols](#))
- Resection of isolated retroperitoneal recurrence ([Shibata and cols](#))

- Effect of salt and water balance in post-operative intestinal function ([Lobo and cols](#))
- Utility of pre-operative CT scan in colon cancer ([Barton and cols](#))
- Transanal excision after rectal cancer downstaging by pre-op chemoradiotherapy ([Schell and cols](#))
- Impact of socioeconomic deprivation in surgery for colorectal cancer ([Hole and cols](#))
- Sexual and urinary function after total mesorectal excision ([Pocard and cols](#))

4. Adjuvant therapy

Fourteen papers about adjuvant therapy were included in this review. Few topics seem to concentrate the attentions:

The role of adjuvant therapy in elderly

Three papers included studied this still controversial subject ([Neugut and cols](#), [Magne and cols](#) and [Fata and cols](#)).

Irinotecan

Three studies have assessed the role of this drug in colorectal cancer in outpatient therapy for metastasis with cisplatin ([Shimada and cols](#)), in European adjuvant trials ([Douillard and cols](#)) and associated to 5-FU and folinic acid for metastatic disease ([Cunningham and cols](#))

Preoperative radiotherapy

Despite crescent evidences of benefits achieved by pre-operative chemoradiotherapy great variation may be observed among schedules used by different centers. A contribution for this discussion may be found in a report by [Basha and cols](#) where a experimental study was undertaken to compare three preoperative radiation regimens for resectable rectal cancer. In other paper, results of a short-course preoperative radiation therapy for operable rectal cancer is presented by [Tankel and cols](#).

Other studies:

- Costs and consequences of chemotherapy for metastatic colorectal cancer ([Hale and cols](#))
- Multicentric randomised comparison of three chemotherapy regimens in metastatic colorectal cancer ([Maughan and cols](#))
- Achievements in advanced colorectal cancer in Europe ([Bleiberg and cols](#))
- Celecoxib with chemotherapy ([Blanke](#))
- Predictors of response to 5-FU in advanced colorectal cancer ([Massacesi and cols](#))

5. Metastatic disease

Liver metastasis

Different aspects of colorectal cancer liver metastasis were studied in six papers included in this review. Parameters for adequate margins for resection of metastasis were studied by [Kokudo and cols.](#) The role of hepatic arterial infusion chemotherapy was reviewed by [Kemeny](#) and [Clavien and cols.](#) Benefits of aggressive treatment of liver metastasis by second resections were analyzed by [Petrowsky and cols.](#) The mode of infiltrative growth was determined by [Yamaguchi and cols](#) as a useful predictor of recurrence after liver resection and trends in long term survival were studied by [Choti and cols.](#)

Lung metastasis

[Ike and cols](#) reported results of an aggressive resection approach of lung metastasis detected by an intensive follow-up.

Selected Abstracts

Molecular biology and colorectal cancer markers

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Staging, follow-up and screening of colorectal cancer

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