“Epidemiology Key points”

- Colorectal cancer (CRC) is the third most frequent cancer in both sexes combined in Europe, after prostate and breast cancer. Around 30% of all CRC cases are diagnosed in the rectal anatomic site.
- In European countries incidence is stable or decreasing. CRC relative survival was 53.5% in both sexes. The lowest relative survival being observed in Poland and in the Czech Republic whereas the highest was observed in Switzerland, Norway and Sweden.
- The key risk factors identified for colorectal cancer as an entity are dietary components, physical exercise, obesity and alcohol, as well as some medical therapies.
- A proportion of colorectal cancer (around 5-10%) are inherited in autosomal dominant predisposition: familial adenomatous polyposis (FAP) and Hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome. Individuals with a first degree relative with colorectal cancer have approximately a two-fold risk of developing colorectal cancer.
- Faecal occult blood test screening for colorectal cancer has been shown to be effective in reducing mortality in a screened population.

“Diagnostic Imaging Key points”

- There is an increasing role for imaging in the preoperative locoregional staging of rectal cancer. The challenging task at present for preoperative imaging in rectal cancer is the identification of subgroups of patients with different risk for local recurrences, so that these patients can be stratified into a differentiated treatment strategy.
- The Tumor Stage: Endorectal ultrasound is very accurate for selection of superficial (T1 versus T2) rectal tumors from the more advanced one, but performs less well in staging advanced rectal cancer, T3 or T4 tumors. Phased array MRI has difficulty in the differentiation between T1 versus T2 lesions and between T2 versus borderline T3 lesions with overstaging as the main cause of errors, but is highly accurate in staging advanced rectal cancer.
- The Circumferential resection margin (CRM): MRI is highly accurate for the prediction of the CRM. Modern multislice CT is more available and faster in acquisition than MRI, however for low rectal cancer 4-16 slice CT is not sufficiently accurate incurring many over and understaging errors for prediction of a free or involved resection margin.
- The Nodal Stage: Identifying nodal disease is still a diagnostic problem for the radiologist. CT cannot accurately distinguish between malignant and benign lymph nodes. EUS was only slightly superior to non contrast enhanced MR and CT. MRI with lymph node specific contrast enhancement may be the most promising modality. FDG PET have so far shown disappointing results for N-staging in rectal cancer.
- Imaging after chemoradiation therapy: For the selection of (non-) responders after neoadjuvant chemoradiation therapy FDG-PET has a wider role. Restaging with MRI results in many errors, especially downstaging to superficial tumors ypT0, ypT1,ypT2 was very inaccurate when the tumour has become fibrotic. The detection of small clusters of residual tumour cells among fibrosis remains a problem.

“Pathology Key points”

- Careful macroscopic and microscopic examination of the rectal cancer specimen is vital to auditing the quality of pre-operative imaging, auditing surgical technique, assessing prognosis and selecting the best adjuvant therapy. Following pre-operative radiotherapy this presents particular challenges to the pathologist but a standardized approach to these specimens will allow proper
comparisons to be made between different neoadjuvant protocols and assessment of new prognostic factors such as regression grade.

"Surgical Key points”

- Loco-regional tumor control in rectal cancer surgery has changed dramatically during the past 10-15 years. The standard surgical technique is currently Total Mesorectal Excision (TME). In patients with a tumor in the middle or distal third of the rectum, a TME is always indicated.
- It has been claimed, mainly based upon historical controls, that radio-(chemo)therapy with delayed surgery will increase the number of preserved sphincters due to a downsizing effect on the tumor allowing more conservative surgery in the lower third of the rectum. Unfortunately, there are no randomized trials supporting this idea. Furthermore, sphincter preservation without good function is of questionable benefit, although many patients from the Mediterranean areas will accept poor bowel function in preference to a stoma.
- Pathological studies of the CRM at the level of the anorectal junction and anal canal sphincter show higher rates of CRM involvement due to dissection along the thinning mesorectum on to the anal sphincter.

“Radiotherapy and Chemotherapy Key points”

- Early localized tumors can be adequately treated with a variety of local therapies such as local excision or endoluminal radiotherapy. If a patient is offered a local surgical strategy, it is important to validate the quality of the specimen as well as adverse pathological factors.
- More than 15 randomized trials and three meta-analyses revealed a decrease in local recurrence, whereas conflicting results for survival advantage are still reported. A systematic review of radiation therapy trials indicates that survival is improved by about 10% using preoperative radiotherapy. Preoperative therapy has gained wide acceptance as standard therapy for rectal cancer.
- It is not possible to accurately compare the local control and survival outcomes of short-course preoperative radiation with conventional preoperative combined modality therapy used more recently, because there is more favourable patient selection in the series using short-course radiation. Subgroup analysis however shows that short-course radiation does not seem effective enough for patients with a predicted positive CRM and possibly low seated tumours.
- Two randomized trials (EORTC 22921, FFCD 9203) have examined whether chemotherapy improves the results of preoperative radiation in patients with cT3-4 rectal cancer. Both studies showed in chemotherapy groups: decrease in local recurrence, an increased rate of pT0 and Grade 3+ toxicity, no benefit of overall survival at 5 years.
- A Polish trial randomized resectable cT3-4 patients to 5 Gy×5 followed by surgery or preoperative chemoradiotherapy. No differences in sphincter preservation, local control, 5 year survival and late toxicity were observed.
- The main advantage of postoperative radiotherapy is better selection of patients based on pathologic staging. No randomized trial of adjuvant post-operative radiation therapy alone has shown an improvement in overall survival. In 1990, the NCI Consensus Conference, analyzing the postoperative North American chemoradiotherapy studies, stated that combined modality therapy was the standard post-operative treatment for patients with pT3 and/or N1-2 disease. Acute toxicity is usually high with postoperative therapy.
- Preoperative and postoperative therapy have been compared in four randomized trials. In the Germany trial (CAO/ARO/AIO 94) the preoperative group had a significant decrease in local failure, acute toxicity, late toxicity, significant increase in sphincter preservation and no difference in 5-year survival. At the present time, patients with cT3-4 rectal cancer who require combined modality therapy should receive it preoperatively.
- There are no firm data with level 1 evidence on the role of adjuvant postoperative chemotherapy after pre-operative treatment with (chemo)radiation, but the accumulation of data from several randomized trials seems to underline an effect of adjuvant chemotherapy.
- Unresectable rectal cancer is a heterogeneous disease: it depends on the extent of the operation the surgeon is able to perform as well as the morbidity the patient is willing to accept. All patients with primarily unresectable disease should receive preoperative combined modality
therapy in the range of 50-54 Gy plus 5FU-based chemotherapy to enhance R0 resectability. Experience of increasing the dose using concomitant or sequential boosts has been reported. Extended surgery is still recommended even if there is a favourable response after preoperative therapy.

- To increase local control a large single dose of radiation is delivered to a surgically exposed area (IORT), while uninvolved and dose-limiting tissues are displaced. North American and European single institution studies support a favourable effect in unresectable patients.
- Patients with local recurrence have a very unfavourable prognosis: the median survival ranges between 1 and 2 years. Attempts to classify localized pelvic recurrences according to the tumor location within the pelvis have been practiced. Patients should receive preoperative combined modality therapy, IORT offers conflicting results. Re-irradiation is under clinical evaluation in recurrent patients previously irradiated.

“Treatment toxicity and quality of life Key points”

- Acute side effects such as diarrhea and increased bowel frequency (small bowel), acute proctitis (large bowel), and dysuria are common during treatment. The symptoms appear to be a function of the dose volume and fraction size rather than the total dose. Delayed complications occur less frequently but are more serious. The initial symptoms commonly occur 6-18 months following completion of radiation.
- There is strong evidence from the literature that bowel function will be further impaired after both preoperative and postoperative irradiation. Some surgical techniques could help preserve bowel function: colonic reservoir construction, stimulated graciloplasty, retrograde irrigation system. Urogenital dysfunction after rectal cancer treatment is often reported, both radiotherapy and surgery contribute to its development.

“Follow-up Key points”

- The main aim of follow-up is to improve survival. Published studies imply that finding extraluminal recurrences (local recurrence after rectal cancer and liver metastases after colorectal cancer) is the main benefit from the follow-up program. The exact value of following patients after radical resection for colorectal cancer is still controversial however. Moreover, the frequency of follow-up is still debatable. Nonetheless, despite sparse evidence, follow-up programmes are being used in most clinics treating colorectal cancer patients.
- Two systematic reviews with meta-analyses were published with the same conclusion: more intensive follow-up decreases mortality in colorectal cancer compared with sporadic or less intensive follow-up. The results of these meta-analyses have been criticised over the quality of surgery, preoperative staging and the intensity of follow-up in the controls, and they should be viewed with caution.

References