ESGE Newsletter

ESGE/ESDO Quality in Endoscopy: Colonoscopy and colonic neoplasms symposium reports

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The European Society of Gastrointestinal Endoscopy (ESGE) and the European Society of Digestive Oncology (ESDO) joined forces for this second symposium in the Quality in Endoscopy series and invited leaders in the field of colonoscopy and colonic neoplasms, alongside young rising stars. Sixty-seven abstracts were submitted and 30 were finally accepted. Over 200 endoscopists attended the symposium. The meeting took place in a modern and very convenient location with high-quality video facilities, which allowed excellent illustration of the case presentations and stimulated the debates. All participants and the survey responses indicated that the meeting fulfilled its aim of providing state-of-the-art knowledge of quality in colonoscopy through lectures, case discussion, and interactive participation. The different aspects of quality in colonoscopy were covered from A (bowel cleansing) to Z (stenting), and the social networking was also very fruitful. Indeed, the meeting was so active and productive that it is hard to summarize. One particularly striking feature was the number of young women working as experts in this field and contributing excellent presentations.

Starting at A, then, the initial session focused on patient preparation and, of course, first on bowel cleansing. According to **Brian Saunders**, the basic principles for successful bowel cleansing are clear instructions, dietary restriction for at least 24 hours, a policy of enema administration in the endoscopy unit prior to the procedure in cases of "failed preparation," and, if necessary, mechanical bowel preparation with "jet wash" devices. While the type of preparation required should be tailored to the individual, a split administration regimen with the patient continuing to drink clear fluids until close to the time of the procedure results in a bowel preparation that is better tolerated and more effective. Scoring systems for bowel preparation, such as the Boston Bowel Preparation Scale, are useful for intermittent monitoring of quality, but are probably not necessary routinely outside of clinical trials.

Christian Boustiere then summarized the 2011 ESGE guideline on the management of patients taking antiplatelet agents, and we can only encourage readers to refer to the guideline itself (Endoscopy 2011; 43; 445 – 458). The key factors are the patient's thrombotic risk and the bleeding risk associated with the procedure. New antiplatelet agents were presented and discussed: the bleeding risk associated with their use is higher than with aspirin and clopidogrel and these new drugs must be discontinued 7 days prior to the procedure.

Siwan Thomas-Gibson had the task of recalling the basics of performing colonoscopy and emphasized the need for dedicated training and trainers. While the mainstay of training remains the apprenticeship approach, recent technological innovations have been shown to enhance training. These include not only virtual reality simulators but, above all, the 3 D imager guide.

Michael Bretthauer addressed the hot topic of quality indicators. He distinguished between process indicators (such as polyp and adenoma detection rates, or withdrawal time) and outcome indicators (for example, rates of missed cancer, of interval cancer, or perforation rates). Numerous studies have shown significant variation in the quality of colonoscopies performed, between countries, between centers, and between individual endoscopists, and there is a clear need for colonoscopists to measure and record performance. To date, a minimum standard set of quality indicators should be collected during each colonoscopy. In addition to patient data, clinical indication, diagnosis, and surveillance strategy, these indicators include: bowel cleansing regimen and quality; sedation; endoscope and equipment used; time to reach the cecum; withdrawal time; polyp, adenoma, and cancer detection rates; complications and adverse events; and patient discomfort and satisfaction. Very importantly, Michael Bretthauer stated that the responsibility of care providers in terms of follow-up quality assurance programs should be guided by the principle "improvement, not punishment."

To clarify terms before the Great Debate on mass screening for colorectal cancer, **Thierry Ponchon** stratified the risks of colorectal cancer. Persons at average risk of colorectal cancer (sporadic cases) should be monitored within an organized mass screening program. Those at high risk of colorectal cancer (nonsyndrome familial cases, irritable bowel disease) represent 10 % – 30 % of colorectal cancer cases and should be followed up directly by colonoscopy. For those at very high risk of colorectal cancer (familial syndrome-related risk: familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer), who represent 3 % of cases, monitoring is based on oncogenetic consultation, the search for mutations, and regular chromocolonoscopy.

The speakers in the Great Debate on mass screening were **Jaroslaw Regula**, **Adam Haycock**, and **Thomas Seufferlin**. In Europe, mass screening is mainly based on guaiac or, increasingly, immunochemical fecal occult blood testing. First-line colonoscopy or rectosigmoidoscopy are used or under evaluation in some countries (such as Poland and Germany for colonoscopy, UK and Italy for rectosigmoidoscopy). New biological tests are also under evaluation and, provided they are less expensive, could be in use in a few years' time.

Michal Kaminski was charged with telling the truth about the limitations of diagnostic colonoscopy. Missed colorectal cancers represent 3.4 % – 7.9 % of all colorectal cancers. Three reasons could explain these interval colorectal cancers: rapid growth of colorectal cancer, incomplete removal of polyps, or overlooked polyp or colorectal cancer. Rapid cancer growth could result from alternative colorectal cancer pathways (such as microsatellite instability). Incomplete endoscopic resection could contribute one-third of missed colorectal cancers and explain why missed lesions occur more frequently in polypectomy segments. However, overlooking lesions at colonoscopy is the major factor, even with the more recent endoscopes. It has been shown that a higher rate of detection of adenomas is associated with a reduced risk for interval colorectal cancer. Polyp location behind folds, subtle lesions that are unrecognized or unfamiliar, poor bowel preparation, and incomplete colonoscopy are the factors that contribute most significantly to the overlooking of lesions. Picking up the thread, **Michael Vieth** and **Ana Ignjatovic** described the histological and macroscopic features of some of the "new lesions" which can easily be overlooked: sessile serrated lesions, lateral spreading tumors, depressed carcinomas.

In his lecture on quality control, **Roland Valori** was emphatic that some parameters of quality control can only be reported at regional or national levels, thus underlining the role of care providers in establishing quality assurance programs on a regional or national basis such as in the UK.

Since everybody in the audience was convinced that we should detect adenomas better, the question was how to do it: through better technology, as suggested by **Ralph Kiesslich**, or simply through better technique, as suggested by **James East**? In the large majority of studies, up to now, new technologies have not been demonstrated to be effective in improving the adenoma detection rate. On the other hand, operator performance varies 10-fold for adenomas of all sizes and three- to four-fold for advanced adenomas. So it appears obvious that operator technique should be optimized before new technology is added. James East focused on bowel preparation, withdrawal time (although its exact role is debated), position changes, use of antispasmodics, and rectal retroflexion. In conclusion, with regard to adenoma and colorectal cancer detection, priority should be given to better technique and to quality control programs.

Whereas technology has not been demonstrated to be effective in improving adenoma detection, its role in the characterization of polyps has been highlighted, and was especially so during the second Great Debate, "I characterize" versus "I remove," spoken to by **Ana Ignjatovic** and **Raf Bisschops**. On the one hand, either of these approaches to diminutive polyps – whether "diagnose and discard" or "diagnose and leave behind" – has the potential to reduce the cost of histopathological analysis and to save time. One reason for this is that the clinical significance of diminutive polyp (high-grade dysplasia rate) is very low. First studies have shown that invivo optical diagnosis could be an acceptable strategy to assess surveillance intervals without histopathology. On the other hand, though, the discard policy has some limitations, especially in the case of sessile serrated lesions. Thus, the discard strategy should be applied with caution in patients with polyps 6 – 9 mm in size and in those with right-side lesions, because of their malignant potential.

Some time during the meeting was given to new advances in the management of advanced colorectal cancer. **Thomas Seufferlein** summarized the emerging role of targeted therapies. Systemic treatment of colorectal cancer has made consid-

erable progress due to new chemotherapeutic agents, but also due to the so-called "targeted therapies." These agents target the epidermal growth factor (EGF) receptor tyrosine kinase, the vascular endothelial growth factor and, more recently, also multikinase inhibitors. There is thus a need to define patients who will benefit from these therapies ("personalized cancer treatment"), partly because these agents are expensive. Various markers have been identified, such as *KRAS* mutation status, which is now routinely examined. Tumors bearing a *KRAS* mutation do not respond to anti-EGFR antibodies. Other markers such as *NRAS* mutation, *BRAF* mutations, and epiregulin and amphiregulin, two ligands of the EGF receptor, are also under the scope. In contrast to anti-EGF receptor agents, there is little data on markers for antiangiogenic strategies. With the advent of many more novel "targeted" therapeutic strategies for colorectal cancer (e.g. Multikinase inhibitors such as regorafenib), identification of companion markers to select patients who could benefit from these targeted agents is becoming a major challenge.

Jaap Stoker is well known for his contribution to the development of CT colonography and he was tasked with imagining the future of this technology. Meta-analyses of CT colonography in symptomatic patients show that CT is a good alternative to colonoscopy. Jaap Stoker, however, admits that, given the seemingly higher prevalence of flat lesions and the lower accuracy of CT colonography for flat lesions, the technique has limitations. Furthermore, as CT colonography does not provide histopathological analysis and has no therapeutic role, it has to be considered as a triaging technique. It is thus most suited to populations with a relatively low incidence of relevant lesions or those in whom colonoscopy cannot be performed (contraindications to sedation, refusal) or in patients with incomplete colonoscopy. For surveillance, CT colonography is also an alternative to colonoscopy.

CT colonography is above all potentially an important screening method, as it has been demonstrated that the participation rate in a mass screening program using CT colonography is significantly higher than the rate when colonoscopy is used. The technique of MR colonography is less well established than that for CT colonography. Results are comparable to those of CT colonography, but the data for 6 – to 9-mm polyps are not well established. The greatest potential for the technique is its possible future use for molecular imaging (polyp characterization).

The potential role of the colon capsule was also discussed in a heated Great Debate (the third) between **Adam Haycock** and **Cesare Hassan**. Basically, the potential indications for the colon capsule are the same as those for CT colonography (contraindications to sedation, colonoscopy refusal, incomplete colonoscopy) and, as with the latter, the target population is people with a low incidence of lesions. All agree that capsule is a very attractive technology with already interesting results and that more data are needed in terms of the mass screening perspective.

As **James East** pointed out in his presentation on the new colonoscopes, instruments have remained similar for the last 40 years with the exception of electronic video endoscopy. Recently a number of aspects of "push" colonoscopy have been challenged by new devices and instruments. These include the following:(1) Balloon enteroscopy has been successful for previously failed procedures.(2) The concept of avoiding looping by advancing from the tip is used in the Invendo device.(3) An alternative approach to looping is the NeoGuide device in which articulated segments follow each other in a "follow-the-leader" style around colonic angulations.(4)The Aer-O-Scope has an optical head in a balloon that is pushed around the colon by gas pressure. A joystick has replaced the classical bending controllers. Other new advantages include disposability of at least part of the instrument, and the use of light-emitting diodes in the tip to avoid the need for light guides. The Aer-O-Scope provides a 360-degree view of the colonic surface. Nevertheless, taking on the challenges of colonoscopy is not simple: apart from balloon colonoscopy, these new technologies are still under evaluation and some have been abandoned. Therapeutic instruments may also be changing. Dedicated therapeutic platforms have been developed out of the needs of natural orifice transluminal endoscopic surgery research programs that may provide superior tissue manipulation, including triangulation.

Diminutive polyps – **Siwan Thomas-Gibson**'s second topic– rarely harbor advanced pathology, but advanced polyps derive from diminutive polyps. We thus have an opportunity to safely interrupt the pathway to malignant transformation at the earliest phase when the resection carries very low risk. Nevertheless, polypectomy of diminutive polyps must be performed safely and completely. There are multiple therapeutic options. Hot biopsy has gone out of vogue in the UK, explained Siwan Thomas-Gibson, especially proximal to the splenic flexure, because of the risk of delayed bleeding and perforation. These complications are likely to be due to suboptimal technique, and safer options are available. Polyps smaller than 3 mm can be removed using cold forceps, but care should be taken to remove the entire polyp. Slightly larger polyps can be removed by cold or hot snare, with or without lifting solution. Retrieving the histological sample from a diminutive snare polypectomy is frequently and frustratingly difficult. The speaker presented tips for retrieval during her talk.

The session then became totally interactive, with case presentations on difficult polypectomy, endoscopic mucosal resection, and management of bleeding and perforation. Experts had enough time to explain tricks and answer the many questions.

How to manage a malignant adenoma, whether by endoscopy or surgery, was **Evelien Dekker**'s subject. For each individual person the risk of residual disease should be weighed against the risks of the surgical procedure. Risk factors for residual disease and/or lymphatic invasion in the case of endoscopic resection include a positive or unknown resection margin, nonpedunculated morphology, deep submucosal invasion (beyond sm1 in the case of sessile lesions), poor tumor differentiation, and lymphovascular invasion. The pathologist should perform a very precise and complete examination of the specimen, while the operator should advise the patient on the possibility and need for further treatment. Ideally the endoscopist should recognize in vivo that the adenoma may possibly be invasive, so as to prevent the useless performance of a polypectomy with its accompanying risk of complications. This will also offer the opportunity to tattoo the location of the polyp when suspicious for malignancy. The main feature of invasive growth is the Kudo V pit pattern, which must be known by all endoscopists.

"Do we need to learn and perform colorectal endoscopic submucosal dissection" (ESD) is one of the more controversial topics, and it was covered by the fourth Great Debate, between **Alessandro Repici** and **Thierry Ponchon**. ESD aims to get a R0 resection, i.e., one in one piece with a normal margin laterally and in depth. In fact ESD, even when performed by Japanese experts, does not always result in an R0 resection and carries a significant risk of perforation. The two debaters concluded that ESD has a role and should be performed in referring centers. Indications for ESD are adenomas with a carcinomatous component (Kudo V) and adenomas that carry a high risk of carcinomatous component, such as the nonnodular lateral spreading tumor.

The fifth and final Great Debate was on the role of colonic stenting. Indications for colonic stents have broadened from palliation to bridge to surgery, in patients who are potentially operable who have an acute obstruction. In either situation, the main goals are to avoid emergency surgery and stoma creation. The major side effect is the risk of perforation, which results in peritoneal tumor spread and is increased by bevacizumab therapy. Another issue is the risk – so far theoretical – related to circulating tumor cells. Recent randomized studies have generated a debate especially regarding the bridge-to-surgery situation, and this was also a matter of discussion between the debaters, **Alessandro Repici** and **Philippe Rougier**. A multidisciplinary approach to the use of colonic stents is needed – and more randomized studies are still necessary.

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