

Colorectal malignant adenoma: do all high-risk lesions need surgery?

Cesare Hassan¹, Carlo Senore², Alessandro Repici³

1 Endoscopy Unit, Nuovo Regina Margherita Hospital, Rome, Italy

2 AOU Città della Salute e della Scienza S Giovanni Battista-CPO Piemonte, SCDO Epidemiologia dei Tumori, Turin, Italy

3 Gastroenterology Department, Digestive Endoscopy Unit, IRCCS Istituto Clinico Humanitas, Milan, Italy

The advent of population-based organized programs for colorectal cancer screening in Europe—either with the fecal test or endoscopy—will result in the identification of a very high number of patients with advanced neoplasia, when considering the magnitude of the covered population and the efficacy of screening tests in selecting an enriched-disease population.¹ A distinctive character of organized programs is the relatively high prevalence of adenomatous polyps with submucosal invasive cancer—also named “malignant adenomas”. For example, in the Italian screening programs (both those using immunochemical-fecal test and those using sigmoidoscopy), about one-third of the screen-detected invasive cancers are represented by malignant adenomas. Thus, the treatment of such lesions represents a relevant priority in lower-gastrointestinal endoscopy.²

Differently from precancerous adenomatous polyps, the efficacy of endoscopic resection is limited when dealing with malignant adenomas, due to the risk of deep neoplastic penetration in the bowel wall or lymph-nodal/distant metastasis.³ Thus, surgery may be required to complete the removal of the invasive cancer or to appropriately stage the disseminated disease. In order to filter those patients in whom endoscopic resection is ineffective, endoscopic and histological risk factors have been proposed to stratify the risk of post-polypectomy residual local or distant disease. However, such a paradigm has been validated only in a few series, leaving uncertainty as to its efficacy.⁴⁻⁸

In the current issue of this journal, Nałęcz-Janik et al.⁹ reported a large series of 128 patients with malignant adenomas with an adequate duration of clinical follow-up, namely, 70 months. The authors reported a favorable outcome in 92.7% of the cases with a limited exploitation of postpolypectomy surgery (28.1%).

The paper Nałęcz-Janik et al.⁹ presents several points of strength. First, the same protocol has been prospectively applied in the same center, so that the same algorithm has been proposed to all patients, assuring uniformity to a long-lasting series (the enrollment encompassing over 20 years). Secondly, a multidisciplinary protocol was adopted, including not only endoscopic surveillance, but also periodical biochemistry and radiological assessment. Third, a very high compliance with the proposed algorithm in the low-risk group was observed, when considering that 93% of low-risk malignant adenomas were managed conservatively (ie, without surgery) and followed up clinically. Thus, the study provided adequate information on this group, which represents by far the most critical issue in this topic. The fact that apparently less than 50% of those patients in whom surgery was recommended actually undertook it was not unexpected. Indeed, the refusal of surgery was mainly due to the high risk of surgery-related morbidity and mortality in elderly patients or those with comorbidities. Of note, such a relatively low rate of surgery referrals allowed the authors to collect information on the long-term clinical follow-up of patients with high-risk malignant adenomas treated conservatively. Fourth, the authors tested 2 different categories of criteria to stratify malignant adenomas, namely, the classic criteria (ie, <2 mm margin-free resection, lympho-vascular invasion, and poor differentiation) and a more modern set, including tumor budding and a 1-mm threshold for the margin-free resection at pathology. Both criteria showed optimal performance, with the latter further reducing the need of surgery. Fifth, the absolute number of unfavorable outcome, namely, 10 cases, allowed the authors to detail the characteristics of such population, including the presence or absence of the single risk factors.

The main results of the study are of high clinical interest. The authors showed the adequate

Correspondence to:

Cesare Hassan, MD, Endoscopy Unit, Nuovo Regina Margherita Hospital, Via Morosini 30, 00153 Roma, Italy, phone: +39-06-58446608, fax: +39-06-58446533, e-mail: cesareh@hotmail.com

Received: April 14, 2015.

Accepted: April 15, 2015.

Conflict of interest: none declared.

Pol Arch Med Wewn. 2015;

125 (4): 225-226

Copyright by Medycyna Praktyczna,

Kraków 2015

clinical predictive value of the proposed protocol, especially of the endoscopic-pathological criteria.⁹ The fact that no patient with low-risk malignant adenoma presented with local or distant recurrence is reassuring, confirming that the efficacy of endoscopic resection is not limited to premalignant lesions, but also to superficial invasive cancers with no unfavorable features. In particular, the distribution of the risk factors among the lesions with unfavorable outcome emphasized the dominant role of the margin-free resection. Indeed, in 8 of 10 unfavorable outcomes, the margin of resection was positive, directly proving the inefficacy of endoscopic resection in removing the entire lesion rather than an intrinsically aggressive behavior of a limited lesion.⁹ It will be interesting to see whether new techniques of endoscopic resection, such as endoscopic submucosal dissection, may further reduce the rate of malignant adenomas with a positive resection margin.¹⁰ The strength of this association was apparently unaffected by the reduction from 2 mm to 1 mm in the definition of the margin-free resection. The fact that adopting less restrictive criteria for classifying margin-free resection might have allowed to avoid surgical referral in some patients without any effect on the likelihood of unfavorable outcomes, would further suggest that more specific criteria for classifying high-risk patients are needed to reduce the risks associated with unnecessary surgery. The outcome of patients with malignant adenomas at high risk also deserves further consideration. The overall prevalence/incidence of an unfavorable outcome was limited to no more than 15% of the cases, suggesting that the majority of patients were already cured by endoscopic resection, so that no benefit could be expected by an additional surgery. Indeed, surgery does not necessarily mean a definitive cure from the invasive cancer, as shown by the equivalence rate of unfavorable outcomes, irrespectively of whether the patients underwent surgery or not.⁹ This would support a more conservative approach in such a category, including a possible restratification despite the higher risk of persistent local or distant disease. In particular, a possible restratification may be based on the risk of morbidity/mortality related to surgery. Based on large prospectively collected surgical series of patients operated on for an already-developed colorectal cancer, patients may be classified at low-, intermediate-, or high-risk of colorectal surgery with a high degree of reproducibility and generalizability.¹¹ Subsequently, it would appear reasonable to reserve surgery only to those patients with a low risk of surgery, endoscopy to those with high surgical risk, and to cautiously assess case by case in those with an intermediate risk.

The series presented by Nałęcz-Janik et al.⁹ also has some limitations. It did not include randomization in the high-risk group, so that we cannot exclude selection bias in the choice between surgical or conservative approach. Secondly, the lack

of statistical significance for the role played by tumor budding may be simply related to the relatively small sample size, due to the low frequency of this feature in the presented series. The role of budding has been consistently showed in the colorectal cancer field, so that it is advisable to include it in the modern treatment of these lesions. Third, the endoscopic classification of Paris was not yet available at the time of the initial enrollment,¹² so that it remains unknown whether a further subclassification could have been allowed by polyp morphology.

In conclusion, the series by Nałęcz-Janik et al.⁹ further reduces the uncertainty on the treatment of patients with low-risk malignant adenomas, in whom additional surgery does not seem to play any role, while opening the door for more conservative strategies for those patients with high-risk malignant adenomas who are also at high-risk of surgery.

REFERENCES

- Hassan C, Giorgi Rossi P, Camilloni L, et al. Meta-analysis: adherence to colorectal cancer screening and the detection rate for advanced neoplasia, according to the type of screening test. *Aliment Pharmacol Ther.* 2012; 36: 929-940.
- Zorzi M, Fedato C, Grazzini G, et al. [Screening for colorectal cancer in Italy, 2010 survey]. *Epidemiol Prev.* 2012; 36: 55-77. Italian.
- Hassan C, Zullo A, Risio M, et al. Histologic risk factors and clinical outcome in colorectal malignant polyp: a pooled-data analysis. *Dis Colon Rectum.* 2005; 48: 1588-1596.
- Hassan C, Pickhardt PJ, Di Giulio E, et al. Value-of-information analysis to guide future research in the management of the colorectal malignant polyp. *Dis Colon Rectum.* 2010; 53: 135-142.
- Geraghty JM, Williams CB, Talbot IC. Malignant colorectal polyps: venous invasion and successful treatment by endoscopic polypectomy. *Gut.* 1991; 32: 774-778.
- Netzer P, Forster C, Biral R, et al. Risk factor assessment of endoscopically removed malignant colorectal polyps. *Gut.* 1998; 43: 669-674.
- Cooper HS, Deppisch LM, Gourley WK, et al. Endoscopically removed malignant colorectal polyps: clinicopathologic correlations. *Gastroenterology.* 1995; 108: 1657-1665.
- Cranley JP, Petras RE, Carey WD, et al. When is endoscopic polypectomy adequate therapy for colonic polyps containing invasive carcinoma? *Gastroenterology.* 1986; 91: 419-427.
- Nałęcz-Janik J, Zagórowicz E, Bartnik W, et al. Outcomes of endoscopic polypectomy for malignant adenomas: a prospective 30-year cohort study from a single center (STROBE 1a). *Pol Arch Med Wewn.* 2015; 125: 272-281.
- Repici A, Hassan C, De Paula Pessoa D, et al. Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review. *Endoscopy.* 2012; 44: 137-150.
- Tekkis PP, Kassaris N, Kocher HM, et al. Evaluation of POSSUM and P-POSSUM scoring systems in patients undergoing colorectal surgery. *Br J Surg.* 2003; 90: 340-345.
- The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. *Gastrointest Endosc.* 2003; 58: S3-S43.