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Editorial

Metachronous rectal cancer after surgery for familial adenomatous polyposis: what should we expect?

Familial adenomatous polyposis (FAP) is an autosomal dominant inherited syndrome characterized by multiple adenomatous polyps (predisposing to colorectal cancer development) and numerous extra-colonic manifestations. It may affect up to 8 per 1000 persons. If not treated by prophylactic colectomy, FAP patients will have an estimated 100% risk of developing colorectal cancer (CRC). The majority of FAP patients will be affected in a context of familial history. However, almost 30% may have a "de novo" mutation. Classic FAP and its attenuated form (AFAP) derive from germline APC (adenomatous polyposis coli) gene mutations.

In an ideal scenario, the majority (if not all) of FAP patients should undergo surgery as result of effective surveillance, being operated on while still asymptomatic. Therefore, the most important objective to be accomplished is CRC prevention. Surgery represents the sole means of preventing CRC, through restorative proctocolectomy (RPC), or through total colectomy with ileorectal anastomosis (IRA). Apart from obvious, it is widely known that RPC is associated with increased early and late morbidity. On the other hand, it is more effective than IRA to prevent occurrence and mortality from rectal cancer in patients with FAP undergoing prophylactic surgery. Notwithstanding, making the choice between RPC and IRA continues a matter of debate. Therefore, the paper published by Stevanato Filho et al. in the present issue of JCOL represents a very important contribution about defining surgical options in FAP. In a retrospective single-institutional analysis of 22 patients with classic FAP, the authors reported complications occurring in 34.3%, although with no mortality. Ultimately, the incidence of rectal cancer after RPC and after IRA was 2.3% and 18.8%, respectively. Given these results, what should be the expected CRC occurrence for FAP patients undergoing surgery after genetic counseling and regular clinical follow-up? It should be warned that a crude answer may not be available at the end of this editorial.

IRA is currently recommended for patients with few rectal polyps with high risk aversion and also for female patients willing to be pregnant. IRA is associated with favorable surgical and functional outcomes and a metachronous rectal cancer rate of less than 15% in the post-RPC era.[1,2] It is estimated that after IRA, metachronous rectal cancer risk is associated with the length of postoperative follow-up and the site of APC mutation.[3,4] It is also hypothesized that bad selection criteria would account for a rate of metachronous rectal cancer after IRA above 15%. Nevertheless, maybe bad selection criteria are not the major cause for a possibly high incidence of rectal cancer after IRA. Perhaps, for a subgroup of patients with manifest indications of IRA, it will be unfeasible to prevent the occurrence of metachronous rectal cancer without additional information derived from mutation analysis. Maybe this is a reason why, during the last decades, RPC progressively turned out to be the most common operation despite its surgical morbidity and need for technical expertise.

It has been well established that there is a link between the site of mutation of the APC gene and some features of the phenotype of FAP. This is the so-called genotype–phenotype correlation. What is the impact from mutation analysis on surgical decision for FAP patients? In a study comprising data from four national polyposis registries, according to previously described genotype–phenotype correlations, 475 patients were divided into three genotype groups predicting attenuated, intermediate, and severe polyposis phenotypes.[5] In this study, the risks of proctectomy 20 years after prophylactic colectomy were 10%, 39%, and 61% in the attenuated, intermediate, and severe genotype groups, respectively. Moreover, risks of metachronous rectal cancer after colectomy were 3.7%, 9.3%, and 8.3%, respectively, in the three groups. It is our view that mutation analysis resulted in a very acceptable profile of CRC prevention for patients with FAP undergoing prophylactic colectomy and rectal preserving-surgery.

However, how does this result compare to clinical decision making without mutation analysis remains unknown. Therefore, the results published by Stevanato Filho et al. in the present issue may represent evidence toward a need for broader use of genetics-based surgical decision. Unfortunately, until there, mutation analysis will remain unavailable to many surgeons and institutions.

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