

CHAPTER 12

Complications of Neoadjuvant Treatment

The indication of RT always carries an additional risk of complications that makes a careful selection of patients necessary, in order to avoid overtreatment and the exposure of those who will not benefit.³⁴ Although RT beneficial effects are currently well known in terms of eradication of the disease, the complications that occur after its application are also increasingly recognized.

In order to compare the toxicity of the various treatment regimens, the following scale is used:

Toxicity scale

G° 0 = absence of toxicity.

G° 1 = mild toxicity.

G° 2 = moderate toxicity.

G° 3 = severe and undesirable toxicity.

G° 4 = life-threatening or severely disabling toxicity.

G° 5 = toxic death.

Among the sequelae and complications of neoadjuvant therapy, the most frequent are related to wound healing disorders, not only at the perineal level after APR but also at the anastomotic level, increasing the risk of dehiscences and causing actinic proctitis and enteritis that can lead to anastomotic strictures.³⁷ Long-term complications include abscesses and fistula formation, strictures, mucus discharge, urgency, tenesmus, diarrhea, increased risk of cancer, and more commonly, bleeding. These latter complications are more frequent when RT is administered postoperatively, a fact that was demonstrated by Sauer et al. study.¹⁹⁸ Although most patients have multiple symptoms, one is usually dominant. The treatment can be simple, with local application of corticosteroid enemas or barrier protectors such as sucralfate, although the symptoms usually reappear when their use is discontinued. Endoscopic treatments, such as the application of argon plasma, have also been tried, and on some occasions this condition may motivate surgical treatment, which could include a difficult resection or a definitive ostomy.¹⁰⁵

It is known that RT affects sphincter function causing not only manometric alterations, but also a greater risk of incontinence.¹³² In the same way that APR generates greater functional alterations than anterior resection, a higher frequency of postoperative sexual dysfunction has also been described in patients undergoing RT as part of rectal cancer treatment compared to non-irradiated patients. But the interesting findings of the German Trial has shown a significant reduction in anastomotic stenosis with preoperative vs. postoperative CRT (2.7% vs. 8.5%).¹⁹⁸ It has been evaluated

in important populations that a wait of up to 11 weeks does not increase complications. However, the trial known as GRECCAR-6 showed that a wait of 11 vs. 7 weeks caused a higher number of predominantly medical complications without a significant difference in the number of pCRs.¹²⁹

Postoperative bowel function after low colorectal anastomosis is often imperfect: some patients have varying degrees of fecal incontinence, incomplete evacuation, or excessively frequent bowel movements. But RT often makes such symptoms worse. The construction of a neo-rectum with a J-pouch or a coloplasty was described in order to improve some postoperative intestinal symptoms, although without definitive results.¹³³ In this sense, sacral neuromodulation is a therapeutic strategy that appears promising. Furthermore, the irradiation technique has also improved minimizing the exposure of the anus and intestine within the radiation field. In the future, trials will need to include detailed assessment of quality of life and patient preferences, which will have to be considered in decision-making. As already mentioned, an additional difficulty after neoadjuvant treatments is related to the complexity of identifying lymph nodes in the pathological study of the specimen, since the lymphatic tissue, as occurs with the tumor, is replaced by fibrosis.^{143,219,248}

On the other hand, it has been observed that functional urogenital disorders are also frequent in irradiated patients. The effect of RT aggravates the sequelae that surgical intervention can cause regarding bladder evacuation and sexual potency.¹¹

Finally, the appearance of TNT has also placed systemic ChT in the consideration of the IDT, even in patients without risk of metastatic disease, for example, in order to increase the response and avoid amputative surgery or even a low anastomosis. It should not be forgotten that chemotherapeutic agents are not exempt from toxicity, which can sometimes leave sequelae and in extreme cases cause the death of the patient.

Neoadjuvant therapy saves lives, but it can also put them at risk and seriously alter the quality of life of patients. Therefore, although all the evidence shows that the indication of RT and/or ChT is always necessary, it is more beneficial when applied before surgery. Overindication should also be avoided, to prevent the consequences of unnecessary treatments.