Gastric Cancer Surgery. How Significant is the Progress?

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In 1971 Richard Nixon declared war on cancer. It's interesting to note that military terms are often used in oncology: treatments are "aggressive", there are therapeutic "strategies", receptor's "blockade", or "treatment lines" and chemotherapy drugs "attack" cancer. Well, Nixon's commitment to "defeating cancer" could not be honored. Moreover, still using military terms, we have to quote journalist Sharon Begley: "We fought cancer ... and cancer won" (1). Is her skepticism exaggerated? What is the actual situation in the field of gastric adenocarcinoma treatment, an area where enormous amounts of money have been invested, great progress has been made in understanding tumor biology, and crucial therapeutic successes are claimed, like chemotherapy, minimally invasive surgery, lymphadenectomy and many others? Are they just illusions, forms of marketing, or have they really brought a benefit in survival rates and quality of life for real patients, not just for those in clinical trials?

Obviously, D2 lymphadenectomy, following the Japanese model (with some nuances regarding the preservation of spleen and pancreatic tail), was internationally adopted. After a period of hesitation, due mostly to European studies showing a higher rate of complications for D2 lymphadenectomy - albeit with some design problems, this surgical technique started being considered safe worldwide in 2006 (2). D2 lymphadenectomy is widely used in surgical practice in Romania as well (3-5). There is no consensus on the minimum number of nodes to be dissected: 15, 20, 29 or more than 30 (6)? But we already know that it is preferable for an accurate assessment, to dissect the lymph nodes "ex vivo", on the fresh resection specimen, immediately after surgery (7). Generally speaking, we agree with the Japanese authors: "Dissect as many lymph nodes as possible and you will be rewarded" (8).

Minimally invasive surgery has also gained ground in the field of the gastric adenocarcinoma treatment (9-13). The widespread use of laparoscopy in Southeast Asia has been clearly favored by the high incidence of early gastric cancer (EGC) in Japan, South Korea and China. High accuracy studies, based on impressive statistics, have also argued for laparoscopic radical gastrectomy even in therapeutic guidelines. Things are not as clear in locally advanced gastric cancer (LAGC) as in EGC. However, short-term benefits are demonstrated for this category of patients as well. More recently, in the world of digestive oncology, supported by the popularity gained for the surgical treatment of prostate and gynecological cancers, robotic surgery has entered the field of LAGC. It competes with laparoscopy in the surgery of EGC, where it brings advantages in terms of lymphadenectomy and some benefits in robotic over laparoscopic anastomoses. Robotic surgery, with a better ergonomics, surgical dexterity, and improved stable 3D high-definition visualization, may overcome some technical challenges of the laparoscopic approach. It gained acceptance in EU and in USA as well as in Romania (12). However, we must observe again the lack of data from randomized clinical trials in this matter.

The aggressive biology of gastric adenocarcinoma justifies the inclusion of systemic treatments in the therapeutic protocol. The main methods are preoperative chemotherapy and postoperative adjuvant chemotherapy. Some new therapies have yielded promising results, such as trastuzumab or ramucirumab. There are important regional differences: preoperative chemotherapy is more popular in Europe and the US while postoperative adjuvant chemotherapy is preferred in Asia (14). In either the preoperative or the post-operative administration, chemotherapy seems to increase the cure rate in clinical trials by less than 10%. In metastatic LAGC the therapeutic impact is even more limited and the indications are mostly empirical and not based on the evidence provided by randomized controlled trials. "A new player on the stage" is immunotherapy with check-point inhibitors, that dramatically ameliorated

the survival of patients with melanoma and "non-small cell lung cancer" (14). However, the approach has yielded modest results in the therapy of LAGC. The extremely high price of checkpoint inhibitors requires predictive and/or prognostic biomarkers for their effective indication. Harada et al concludes very suggestively: "Clearly, more basic research is needed to identify novel targets and drugs" (14).

The temporal trends in death rates are considered the most reliable measure of progress against cancer (15,16). Although age-standardized cancer death rates in the USA have been decreasing since the early 1990s, some reviewers cite limited improvement in death rates as evidence that "the war on cancer", which was initiated in 1971 by President Nixon's administration, has failed" (15).

A historical approach to the problem in Romania may be useful if we really want to get an idea of the real progress made in the LAGC's surgical treatment. A properly documented study according to the standards of the epoch was published on the basis of the experience of the Fundeni Surgical Department in 1992 (17), and followed by one in 2001 (18). From the same surgical department, two more recent works are available: one published in 2006 and another in the present issue of the journal *Chirurgia* (3,5). A detailed analysis of the data will be the subject of another paper. However, it is safe to say that after 30 years of gastric cancer surgery in the same institution, everything that seems to have been achieved is in fact an improvement in survival at 5 years by 2-3% (unpublished data)! These data are in line with observations on European level (19,20). This seems to be the reality both worldwide and in our country. Let's say, however, that in medicine, as in science in general, spectacular jumps or revolutionary progress are rare. They most often appear on the background of a gradual accumulation of incremental advancement of scientific knowledge.

Achieving high-quality surgery by well trained and specialized surgeons in accordance with the high and sometimes extremely expensive standards of contemporary medicine remains decisive.

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