

NEWS & VIEWS

Precision medicine: Neoadjuvant treatment and laparoscopic rectal cancer resection

Charalabos Batsis, MD.

From the Department of Surgery,
University Hospital of Ioannina,
Ioannina, TK 45110, Greece.

Preoperative chemoradiotherapy has established as standard treatment of advanced non-metastatic rectal cancer. However, some of these patients do not respond to this therapy while they are experiencing adverse effects. In addition to the need for identifying predictive biomarkers for pre-treatment assessment of neoadjuvant efficacy and toxicity, laparoscopic surgery after neoadjuvant treatment has not fully explored.

DOI: 10.2122/gbc.2012.0215

In recent years, total mesorectal excision continues to be the standard treatment of resectable rectal cancer. However, the timing of adjuvant chemotherapy or chemoradiotherapy in the pre-operative or postoperative setting^{1,2} and the choice of minimally invasive surgery with laparoscopic or robotic surgery and open surgery raises again controversy³. With increasing use of laparoscopic surgery there has been skepticism for the safety and efficacy of this patient-friendly approach after neoadjuvant chemoradiotherapy for rectal cancer.

***Correspondence to**
Charalabos Batsis MD, Assistant
Professor
University Hospital of Ioannina, TK
45110, Greece.

T: +302651099694

F: +302651007094

Email: chbatsis@gmail.com

This question is highlighted by Seshadri and colleagues in the January issue of *Surgical Endoscopy*⁴. The authors report the results of a retrospective study comparing short-term outcomes data between 72 patients treated with laparoscopic surgery (LS) and 72 patients treated with conventional open surgery (OS) after neoadjuvant chemoradiotherapy during the same time period. There were significant difference in favor of LS regarding blood loss, time to passing of first flatus and start of normal diet, and hospital stay and only operating time was significantly shorter in the OS group. An analysis of curability resection markers showed more patients with positive circumferential resection margin in the OS group whereas there was no significant difference in the number of lymph nodes retrieved. The authors conclude that laparoscopic surgery for rectal cancer after preoperative chemoradiation is safe and provides better short-term outcomes without worsening oncological outcomes as compared with open surgery.

This study provides interesting clinical data further supporting the wider use of laparoscopic surgery for rectal cancer. It is clear that large-scale, phase 3 randomized controlled trials are needed to establish the risks and benefits of laparoscopic over open surgery

for rectal cancer. As a clinically useful criterion for the efficacy of preoperative chemoradiotherapy is an increased rate of low anterior resection due to tumor down-staging, the fact that only 8 from 72 patients underwent this approach suggests a limited efficacy of adjuvant treatment, a lack of appropriate patients selection or the continuing preference of authors in abdominoperineal resection. In the western world, the rate of laparoscopic rectal anterior resection with TME has substantially been increased improving quality of life⁵⁻⁷. Laparoscopic surgery for gastrointestinal cancer treatment is being increasingly integrated into clinical practice after the solid evidence of its short-term superiority compared to open surgery for colon cancer and similar evidence is to be expected for rectal and gastric cancer adjusting to current standardized criteria and requirements of minimally invasive surgery^{3,8-12}.

The timing (preoperative, postoperative or both) of adjuvant treatment with chemotherapy, radiotherapy, chemoradiotherapy and targeted therapy has now become controversial. For example, a recent analysis of 12 randomized control trials involving 9410 patients with rectal cancer showed a risk reduction of local recurrence of 50% at the cost of a relative

increase of 50% in treatment-related complications². This data emphasize and support biomedical research for developing novel biomarkers for appropriate selection of patients tailored the most effective with fewer side effects multimodal treatment at individual patients.

However, despite initial enthusiasm either with arrays-based methods for gene expression profiling signatures or sequencing single genes as the *KRAS* for mutations-based decisions on cetuximab or panitumumab, more careful well-designed studies failed to provide repeatable results. In the emerging genome, epigenome, transcriptome and microRNAs era revealing a highly complexity of cancer, the development of personalized diagnostics with robustness for clinical applications appears now to be in the right direction. Revolutionary next-generation sequencing technology and innovative living-cells imaging techniques together with advances in systems computational biology and synthetic biology provide now the capacity of understanding structural and functional cancer genome heterogeneity opening new ways for translating robust diagnostic and preventive tools into clinic¹³⁻¹⁸.

References

1. Glynne-Jones R, Kronfli M. Locally advanced rectal cancer: a comparison of management strategies. *Drugs*. 2011; 71(9):1153-77.
2. Fleming FJ, Pahlman L, Monson JR. Neoadjuvant therapy in rectal cancer. *Dis Colon Rectum*. 2011; 54(7):901-12.
3. Nikiteas N, Roukos D, Kouraklis G. Robotic versus laparoscopic surgery: perspectives for tailoring an optimal surgical option. *Expert Rev Med Devices*. 2011; 8(3):295-8.
4. Seshadri RA, Srinivasan A, Tapkire R, Swaminathan R. (2012) Laparoscopic versus open surgery for rectal cancer after neoadjuvant chemoradiation: a matched case-control study of short-term outcomes. *Surg Endosc*. 26(1):154-61.
5. Hottenrott C. Advances and challenges for laparoscopic rectal cancer surgery. *Gastric and Breast Cancer* 2011; 10(2): 106-8.
6. Liakakos T, Roukos DH. Randomized evidence for laparoscopic gastrectomy short-term quality of life improvement and challenges for improving long-term outcomes. *Ann Surg*. 2009 Aug;250(2):349-50.
7. Ziogas D. Cetuximab limitations and renew interest in surgical resection and research advances for improving stage IV colorectal cancer outcome. *Gastric and Breast Cancer* 2011; 10(2): 94-96
8. Liakakos T, Roukos D. Laparoscopic gastrectomy: advances enable wide clinical application. *Surg Endosc*. 2008 Jun;22(6):1553-5.

9. Ziogas D, Polychronidis A, Kanellos I, Roukos D. Laparoscopic Colectomy Survival Benefit for Colon Cancer: Is Evidence From a Randomized Trial True? *Ann Surg.* 2009 Apr;249(4):695-6.
10. Roukos DH. Laparoscopic Gastrectomy and Personal Genomics: High-Volume Surgeons and Predictive Biomedicine May Govern the Future for Resectable Gastric Cancer. *Ann Surg.* 2009 Oct;250:650-1.
11. Katsios GC, Baltogiannis G; Roukos DH. Laparoscopic surgery for gastric cancer: comparative-effectiveness research and future trends. *Expert Rev Anticancer Ther.* 2010; 10(4): 473–6.
12. Liakakos T, Roukos DH. Is there any long-term benefit in quality of life after laparoscopy-assisted distal gastrectomy for gastric cancer? *Surg Endosc.* 2008 May;22(5):1402-4.
13. Roukos DH. Networks medicine: From reductionism to evidence of complex dynamic biomolecular interactions. *Pharmacogenomics* 2011; 12(5): 695-8.
14. Roukos DH, Hottenrott C, Lorenz M, Koutsogiorgas-Couchell S. A critical evaluation of effectivity of extended lymphadenectomy in patients with carcinoma of the stomach. An analysis of early results and long-term survival. *J Cancer Res Clin Oncol.* 1990; 116: 307-11.
15. Roukos DH. “Big” Science: Genome regulatory networks and novel molecular tools to improve health. *Expert Rev Mol Diagn* 2011; 11(2): 123-6.
16. Roukos DH. Chromatin: A key player in complex gene regulation and future cancer therapeutics. *Epigenomics* 2011 Aug; 3(4): 395–9.
17. Roukos DH. Translating epigenetics into an anticancer drug pipeline for solid tumors. *Expert Rev Med Devices.* 2011 Jul;8(4):409-13.
18. Roukos DH. Measurable evidence of miRNAs as regulators of cancer networks and therapeutic targets. *Expert Rev Med Devices* 2011; 8(2): 123-6.