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OPERA and Phase III Trials for Testing the Hypothesis That Planned Organ Preservation is Feasible in Selected Rectal Cancers

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Editorial

Surgery is and will remain the major curative treatment for rectal cancer. Permanent stoma after abdomino-perineal resection (APR) is becoming unusual but even after low anterior resection (LAR) the quality of life is often poor due to bowel movement dysfunction. First line radiotherapy or chemoradiotherapy (CRT) is becoming a popular way of research to achieve clinical complete response (cCR) and organ preservation. Papillon [1] in the 1970s was one of the first to achieve cCR and long term local control using contact X ray brachytherapy (CXB) for T1N0 and Habr Gama [2] using CRT for T2-3 popularized in the 1990s watch and wait (W-W) after cCR. The Lyon R 90-01 randomized trial [3,4] demonstrated that a CXB boost combined with external beam radiotherapy (EBRT) was able for T2 T3 ≤ 5 cm distal rectum in operable patients to increase sphincter and organ preservation.

Presently the world reference for organ preservation is Habr Gama regimen with CRT: 54 Gy with capecitabine. Using this protocol for T2-3 tumor the rate of cCR is between 15 to 40% (depending on tumor size, stage and interval before response evaluation) and the rate of local relapse after W-W is around 25-30% [5-7]. Such an approach is considered as a good option in the ESMO guideline [8]. As rectal adenocarcinoma is quite a radioresistant tumor [9] combining CRT with a CXB boost is an attractive way of research to increase organ preservation. With this combined treatment results achieved in France and UK since 2002 [10-12] show a rate of cCR for T2 T3 <5 cm of ≥ 75% and local relapse in less than 15% of cases with good bowel function. Relapse in the perirectal nodes are <5%.

To demonstrate that a CXB boost is increasing safely the chance of organ preservation the European OPERA trial (ID-RCB 2014-A0 1851-46) was launched in June 2015. Main Inclusion criteria using mainly colonoscopy and MRI: Adenocarcinoma (well-moderately differentiated) T2 T3 a-b <5 cm, N0, M0 distal-middle rectum, operable patient. All the patients received CRT (45 Gy/5 weeks) with concurrent capecitabine (825 mg/ m2 BID). Randomization is between boost with either EBRT (9 Gy/1 week) or CXB (90 Gy/3 fractions). Tumor response (Digital examination, rectoscopy, MRI) is made on week 14 after start of treatment. If cCR is achieved surveillance or local excision is proposed. In case of partial response TME is performed. End point is organ preservation at 3 years and the hypothesis is to increase organ preservation from 20% to 40% in the CXB group (HR: 0.56). Inclusion of 236 patients should end in 2019 with patients from France, UK, Sweden and Switzerland.

Some other trials (Greccar 12, Star-Tec, Prospect) are testing the possibility to achieve organ preservation using CRT and neoadjuvant chemotherapy. A key point for success is the tumor selection. If large T3 (>4 cm, T3c-d) are included the chance of cCR with CRT alone is less than 15% [13]. On the other hand if T2 and "early" T3 are selected a CRT with CXB boost can achieve a high rate of long term local control and as in anal canal squamous cell carcinoma a planned organ preservation can be proposed to frail patients or if any TME surgery is refused. Long term surveillance is needed as it is possible to see local failure after 5 years which can still be salvaged. A rate of local failure below 15% is the goal if this conservative strategy is not to compromise survival.

As always only randomized trials will bring strong evidence that this combined treatment is providing good and safe organ preservation and could be considered not only as an option but as a standard.

References

1. Papillon J (1975) Intracavitary irradiation of early rectal cancer for cure. A series of 186 cases. Cancer 36: 696-701.
2. Habr Gama A, Gama-Rodrigues J, São Julião GP, Proscurshim I, Sabbagh C, et al. (2014) Local recurrence after complete clinical response and watch and wait in rectal cancer after neoadjuvant chemoradiation: impact of salvage therapy on local disease control. Int J Radiat Oncol Biol Phys 88: 822-8.
3. Gerard JP, Chapet O, Nemoz C, Hartweig J, Romestaing P, et al. (2004) Improved sphincter preservation in low rectal cancer with high-dose preoperative radiotherapy: the lyon R96-02 randomized trial. J Clin Oncol 22: 2404-9.
4. Ortholan C, Romestaing P, Chapet O, Gerard JP (2012) Correlation in rectal cancer between clinical tumor response after neoadjuvant radiotherapy and sphincter or organ preservation: 10-year results of the Lyon R 96-02 randomized trial. Int J Radiat Oncol Biol Phys 83: e165-71.
5. Maas M, Beets Tan RG, Lambregts DM, Lammering G, Nelemans PJ, et al. (2011) Wait-and-see policy for clinical complete responders after chemoradiation for rectal cancer. J Clin Oncol 29: 4633-40.
6. Renehan AG, Malcomson L, Emsley R, Gollins S, Maw A, et al. (2016) Watch-and-wait approach versus surgical resection after chemoradiotherapy for patients with rectal cancer (the OnCoRe project): a propensity-score matched cohort analysis. Lancet Oncol 17: 174-83.
7. Smith JD, Ruby JA, Goodman KA, Saltz LB, Guillem JG, et al. (2012) Nonoperative management of rectal cancer with complete clinical response after neoadjuvant therapy. Ann Surg 256: 965-972.
8. Glimelius B, Tiret E, Cervantes A, Arnold D (2013) ESMO Guidelines Working Group. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 24 Suppl 6: vi81-8.
9. Appelt AL, Pløen J, Vogelius IR, Bentzen SM, Jakobsen A (2013) Radiation dose-response model for locally advanced rectal cancer after preoperative chemoradiation therapy. Int J Radiat Oncol Biol Phys 85: 74-80.
10. Frin AC, Evesque L, Gal J, Benezery K, François E, et al. (2017) Organ or sphincter preservation for rectal cancer. The role of contact X-ray brachytherapy in a monocentric series of 112 patients. Eur J Cancer 72: 124-136.
11. Dhadda AS, Martin A, Killeen S, Hunter IA (2017) Organ Preservation Using Contact Radiotherapy for Early Rectal Cancer: Outcomes of Patients

Treated at a Single Centre in the UK. Clin Oncol (R Coll Radiol) 29: 198-204.

12. Myint AS (2013) Contact radiotherapy for elderly patients with early low rectal cancers. Br J Hosp Med (Lond) 74: 391-396.
13. Gérard JP, Chamorey E, Gourgou-Bourgade S, Benezery K, de Laroche G, et al. (2015) Clinical complete response (cCR) after neoadjuvant chemoradiotherapy and conservative treatment in rectal cancer. Findings from the ACCORD 12/PRODIGE 2 randomized trial. Radiother Oncol 5: 246-52.