Impact of preoperative radiotherapy on survival in locally advanced rectal cancer: an observational population-based study from the South of Switzerland
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Preoperative radiotherapy (RT) followed by surgery is widely accepted in the treatment of locally advanced rectal cancer (LARC). This study aimed to estimate at the population-based level the impact of preoperative RT on overall survival (OS) and cancer-specific survival (CSS) in LARC patients diagnosed in Southern Switzerland between 1996 and 2007. All patients with LARC were selected from the Ticino Cancer Registry database. Patients were categorized according to the first administered treatment: preoperative radiotherapy (RT) followed by surgery (RT+) versus surgery (RT–). Clinical–pathological characteristics and 5-year OS and CSS were analysed. Among 384 patients with LARC, 54% underwent preoperative RT, occurring more frequently in the mid-distal part of the rectum compared with the RT– group (74.8 vs. 29.8%, respectively). Both 5-year OS and CSS significantly improved in RT+ patients (OS: 68 vs. 54%, respectively; CSS: 71 vs. 63%, respectively). The adjusted hazard ratio for all death was equal to 0.66 (95% confidence interval: 0.46; 0.97); similarly, the hazard ratio for cancer-specific death was 0.63 (95% confidence interval: 0.39; 0.99). These observational population-based results, after controlling for most important diagnostic and clinical prognostic factors, confirm the benefit of preoperative RT of LARC, even if the magnitude seems greater than expected in clinical trials results. Additional studies are needed, particularly with regard to the possible effect of standardized staging procedure and multidisciplinary discussion on patient outcome. *European Journal of Cancer Prevention* 21:139–146 © 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Keywords: Cancer Registry, locally advanced rectal cancers, preoperative radiotherapy, survival

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Introduction
Modern multimodal treatment of rectal cancer, associated with multidisciplinary management, has resulted in high control rates, improvements in survival rates and quality of life (Glimelius and Oliveira, 2008; Van Cutsem et al., 2008; Valenti et al., 2009). In particular, the last decade has brought enormous advances in surgical techniques (e.g. total mesorectal excision is now endorsed by all surgeons), chemotherapy (CT) regimens, development of new targeting drugs such as epidermal growth factor receptor and angiogenesis inhibitors and preoperative therapeutic approaches. Considering neoadjuvant treatments, the results of major published randomized clinical trials (RCTs) remained inconsistent and the overall assessment of the preoperative treatment effect was difficult to evaluate until the end of the 1990s. The Swedish Rectal Cancer Trial (SRCT) demonstrated a significant relative survival benefit after a long-term follow-up in the group of patients treated with preoperative radiotherapy (RT) followed by surgery (No authors listed, 1997; Folkesson et al., 2005). Moreover, the SRCT results were compared with the Swedish Cancer Registry findings; authors concluded that the SRCT results were reliable, as the sample of patients included in the SRCT study was representative of the general population, assessing therefore the evidence for the generalizability of the results (Dahlberg et al., 1998, 1999). A recent meta-analysis of 14 RCTs showed that preoperative RT significantly improves 5-year overall survival (OS) and cancer-specific survival (CSS) versus surgery alone in resectable rectal cancers, with a greater benefit in the advanced tumour stages (i.e. Dukes B and C) than in the early stages (Dukes A) (Camma et al., 2000). In another systematic review of 22 trials, the authors found that RT, before or after surgery, essentially reduced the risk of local recurrences and moderately reduced deaths from rectal cancer; however, the benefits detected with preoperative treatment were significantly greater than those with postoperative RT (Colorectal Cancer Collaborative Group, 2001). Similarly, recent data from a German trial showed that preoperative radio(chemo)therapy is superior to postoperative therapy in resectable rectal cancers, in terms of both better local control and less toxicity (Sauer et al., 2004). In contrast, a more recent systematic overview showed late adverse effects because of preoperative RT, although these