Cervical

MRI-guided adaptive brachytherapy in locally advanced cervical cancer (EMBRACE-I): a multicentre prospective cohort study

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BACKGROUND

The concept of the use of MRI for image-guided adaptive brachytherapy (IGABT) in locally advanced cervical cancer was introduced 20 years ago. Here, we report on EMBRACE-I, which aimed to evaluate local tumour control and morbidity after chemoradiotherapy and MRI-based IGABT.

METHODS

EMBRACE-I was a prospective, observational, multicentre cohort study. Data from patients from 24 centres in Europe, Asia, and North America were prospectively collected. The inclusion criteria were patients older than 18 years, with biopsy-proven squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the uterine cervix, The International Federation of Gynecology and Obstetrics (FIGO) stage IB-IVA disease or FIGO stage IVB disease restricted to paraaortic lymph metastasis below the L1-L2 interspace, suitable for curative treatment. Treatment consisted of chemoradiotherapy (weekly intravenous cisplatin 40 mg/m^2, five-six cycles, one day per cycle, plus 45-50 Gy external-beam radiotherapy delivered in 1·8-2.0 Gy fractions) followed by MRI-based IGABT. The MRI-based IGABT target volume definition and dose reporting was according to Groupe Européen de Curiethérapie European Society for Radiation Oncology recommendations. IGABT dose prescription was open according to institutional practice. Local control and late morbidity were selected as primary endpoints in all patients available for analysis. The study was registered with ClinicalTrials.gov, NCT00920920.

FINDINGS

Patient accrual began on 30 July 2008, and closed on 29Dec 2015. A total of 1416 patients were registered in the database. After exclusion for not meeting patient selection criteria before treatment, being registered but not entered in the database, meeting the exclusion criteria, and being falsely excluded, data from 1341 patients were available for analysis of disease and data from 1251 patients were available for assessment of morbidity outcome. MRI-based IGABT including dose optimisation was done in 1317 (98·2%) of 1341 patients. Median high-risk clinical target volume was 28 cm^3 (IQR 20-40) and median minimal dose to 90% of the clinical target volume (D90%) was 90 Gy (IQR 85-94) equi-effective dose in 2.0 Gy per fraction. At a median follow-up of 51 months (IQR 20-64), actuarial overall five-year local control was 92% (95% CI 90-93). Actuarial cumulative five-year incidence of grade 3.0-5.0 morbidity was 6·8% (95% CI 5·4-8·6) for genitourinary events, 8·5% (6·9-10·6) for gastrointestinal events, 5·7% (4·3-7·6) for vaginal events, and 3·2% (2·2-4·5) for fistulae.

INTERPRETATION

Chemoradiotherapy and MRI-based IGABT result in effective and stable long-term local control across all stages of locally advanced cervical cancer, with a limited severe morbidity per organ. These results represent a positive breakthrough in the treatment of locally advanced cervical cancer, which might be used as a benchmark for clinical practice and all future studies.