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Low-dose-rate interstitial brachytherapy boost for the treatment of anal canal cancers

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ABSTRACT

PURPOSE: Evaluate the efficacy and tolerance of interstitial brachytherapy (IBT) after external beam radiotherapy (EBRT) or radio chemotherapy (RCT) for the treatment of anal canal cancers (ACC).

METHODS AND MATERIALS: From 01, 1990 to 01, 2013, 103 patients (p) with ACC were treated with IBT after EBRT or RCT at our institution. Tumor node metastasis stage included Tis (1 p), T1 (18 p), T2 (46 p), T3 (33 p), and T4 (5 p). There was a lymph node involvement in 19 p. Ninety-nine patients presented with squamous cell carcinoma (95.5%) and seven with adenocarcinoma (4.5%). The median EBRT dose was 45 Gy (18−65 Gy). Thirty-nine patients (37.86%) received concomitant RCT. IBT was performed 0.9 months (0−4.38) after RCT or EBRT. The median IBT dose was 17.2 Gy (10−30 Gy).

RESULTS: Within 4.8 years of followup, 15 p (14.6%) had an abdominoperineal amputation with definitive colostomy (11 p had locoregional failure, and 4 p had anal incontinence). Late toxicity was presented in 40 p (38.8%). Overall survival rates of 99% at 1 year, 89.4% at 3 years, and 85.7% at 5 years, and 1-year, 3-year, and 5-year local control rates of 97.9%, 95.4%, and 89.1%, respectively. The 1-year, 3-year, and 5-year colostomy-free rates were 98.9%, 94.0%, and 86.4%, respectively. No factors in the multivariate analysis were associated with the overall survival or any failure type.

CONCLUSIONS: IBT boost provides excellent local control with low colostomy rates and a late toxicity profile in ACC treatment. © 2016 Published by Elsevier Inc. on behalf of American Brachytherapy Society.

Keywords: Anal cancer; Interstitial brachytherapy; Colostomy-free survival

Introduction

Anal cancer is a rare disease accounting for only one to 5% of all colon, rectal, and anal carcinomas (1, 2). Its incidence has drastically increased in the last 2 decades due to anogenital human papilloma virus-related epithelial changes (3). Before the 1970s, radical surgery had been considered the standard therapy for anal cancer with an average 5-year survival rate of 50−60% (4) and late morbidity, such as impotence (54%), intestinal disorders, and psychological or social problems associated with a permanent colostomy (5). External beam radiotherapy (EBRT) alone and the combined radiotherapy and chemotherapy approach (RCT) have been evaluated in the last three to four decades (6). RCT has become a standard treatment for early and locally advanced anal cancer. The combination of RCT and EBRT decreases the local failure rate as well as the radical surgery and colostomy rates (7, 8). EBRT technique has evolved from a classical two-dimensional (2D)-technique to a three-dimensional (3D)-conformal radiotherapy (3D-CRT), and intensity-modulated radiation therapy (IMRT) leads to an improved evaluation of the tumor size and the position of the organs at risk (OAR), allowing for a decrease in the OAR doses. Nevertheless because RCT has become the standard treatment for anal cancer, a boost dose for the primary tumor and techniques for achieving this boost have been

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Conflict of interest: EL, MD, PhD has been acting the chief Medical at Accuray from April 2014 to September 2014.

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discussed. Doses between 36 and 60 Gy in EBRT have been typically delivered to the primary tumor and pelvic and inguinal nodes. Boost approaches for the primary tumor vary from EBRT (electrons or photons) to interstitial brachytherapy (IBT). Usually, IBT is performed 2−3 weeks after of the completion of EBRT. A retrospective series by Papillon *et al.* (9) has shown the efficacy of IBT as a boost treatment and its excellent tolerance; nonrandomized (10, 11) series have shown that a boost with IBT is superior to EBRT in terms of achieving local control (LC) and the colostomy survival rate. In this retrospective series, we analyze that the role of the IBT boost in anal cancer treatment in terms of the colostomy-free survival, LC, regional control (RC), disease control (DC), metastasis-free survival (MFS), colostomy free survival (CFS), overall survival (OS), and to assess long-term toxicity in 103 patients consecutively treated at our institution with EBRT and an IBT boost.

Methods and materials

We examined clinical record from consecutive patients treated from 01, 1990 to 01, 2013, for anal cancer at our institution with EBRT and an IBT boost to the primary lesion because of a good response to EBRT. Initial tumor staging included a clinical pelvic examination with a digital rectal examination, histologic proof of anal cancer and pelvic imaging (echography, abdominopelvic computed tomography scanner, or pelvic magnetic resonance).

External beam radiotherapy

Patients were treated with 2D technique, 3D-CRT, and IMRT; 2D-CRT and 3D-CRT treatment were performed in the supine position with an x-ray ≥ 6 MV delivered in three or four beams. The IMRT technique was performed also in supine position, with helical tomotherapy (Accuray Incorporated, Sunnyvale, CA) and daily megavoltage computed tomography. Energy photons were from 6 to 25 MV (electrons for inguinal nodes were used depending on radiation oncologist criteria). The clinical target volume (CTV) included the entire anal canal with an expansion of 1 cm, which was limited to the external contours of the OAR. The CTV also included the pelvic, inguinal, presacral nodes, and mesorectum. The planning target volume was fixed as a 0.5−1 cm expansion from the CTV.

Chemotherapy

Thirty-nine patients (37.86%) received concomitant chemotherapy.

IBT treatment

The IBT boost application was given to all patients with low-dose-rate [LDR] IBT (192-Iridium). The implantation technique, as originally described by Papillon *et al.* (9), is an interstitial application. Before the introduction of an Arplay applicator (Fig 1), a digital rectal examination was performed to evaluate the tumor response to EBRT. Rigid metal needles are placed in the submucosa space using an Arplay applicator with channel spacing of 10 mm. All applications had a single plane. At the end of the procedure, needles are stuck on the applicator (screw for each channel), and the applicator is stitched to the skin (three to four points). Before the EBRT treatment, the initial tumor was designed in paper schema to guide needle implantation at the time of IBT; 1 cm in all directions was added to create the CTV volume. The dose is prescribed at 85% isodose, which can cover a minimum thickness of 9−10 mm for implantation in only one plane.

Toxicity

Only late toxicity was recorded. Any toxicity that appeared more than 6 months after radiation treatment was considered a late side effect. Toxicity was assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events v4.0 scale. Any grade toxicity was recorded.

Followup and data assessment

Followup consisted of clinical examination every 4 months to evaluate LC and late complications. Radiologic examinations were performed only if there was suspicion of clinical relapse. Patients were then followed up three times per year during the first 2 years and twice yearly thereafter. Only gastrointestinal toxicities were always reported. Others toxicities were self-declared.

Statistical methodology

The SPPS statistics 21.0 software (Statistical Package for Social Science) for windows (an IBM company software, Chicago, IL) was used for statistical analysis.

Fig. 1. Arplay applicator.

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