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Original Research

# Chemoradiation in rectal squamous cell carcinoma: Bi-institutional case series

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Survival;
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**Abstract** ***Background and purpose:*** Primary rectal squamous cell carcinoma (SCC) is an uncommon disease. Early reports stated that surgery is the most effective treatment. However, recent publications suggest conservative strategy with chemoradiation provides satisfactory results.
***Patients and methods:*** We have retrospectively studied the medical charts of 23 patients treated for a rectal SCC in two teaching hospitals in France between 1992 and 2013. Twenty-one patients received an exclusive chemoradiotherapy (CRT) and two a pre-operative CRT followed by a planned surgery. Patients received pelvic irradiation with a dose ranging from 36–45 Gy followed by a boost of 15–23 Gy. Twenty-two patients received a concurrent chemotherapy.
***Results:*** After CRT, the rate of clinical complete response was 83%. With a median follow-up of 85 months, 5-year overall survival rate was 86%. Five patients presented with a relapse. The 5-year disease-free survival rate was 81%. The 5-year colostomy-free survival rate was 65%. Three patients (13%) presented with grade III–IV late rectal toxicity.
***Conclusions:*** Although retrospective, this is the largest cohort of patients treated with CRT for a rectal SCC. Exclusive CRT could result in high local control rate and prolonged survival in rectal SCC patients with a high rate of organ preservation.


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## 1. Introduction

Colorectal carcinoma is the third leading cause of death due to cancer worldwide. Squamous cell carcinoma (SCC) is an extremely rare subtype accounting for 0.1–0.25% of colorectal tumours. First described by Raiford in 1933 [1], 100 cases have since been reported in the literature. The origin of the tumour remains unclear but several theories have emerged. Some authors suggest pluripotent stem cells with an epidermoid differentiation capacity. It has been hypothesised that mucosal aggression, secondary to bowel inflammatory disease, Human Papilloma Virus (HPV) infection, or ionising radiations cause squamous metaplasia underlying tumour development.

Diagnosis requires rectoscopy or colonoscopy with biopsies of visible abnormalities. In 1979, Williams et al. [2] defined conditions to be fulfilled: (1) careful rectal endoscopy to exclude proximal extension of anal cancer, (2) primary SCC ruled out, (3) lack of a fistula tract lined by squamous cells, (4) absence of glandular differentiation.

The best therapeutic strategy for rectal SCC has to be defined. In non-metastatic patients, early reports supported radical surgery as the standard treatment [2,3]. However, based on the experience achieved in anal SCC patients, chemoradiotherapy (CRT) has become the treatment of choice in most of the cases. Radical surgery is limited to patients without response after CRT or at the time of relapse. This retrospective study aims to assess the outcome of patients with rectal SCC treated with CRT in two French university hospitals.

## 2. Patients and methods

### 2.1. Patient selection

Between November 1992 and October 2013, 23 patients with rectal SCC were treated in the Departments of Radiation Oncology in Tenon Hospital, Paris (n = 13) and Besançon University Hospital (n = 10). Patients with tumours involving the anal canal or the ano-rectal junction were excluded. We reviewed retrospectively medical charts of all patients for demographic data, tumour location and stage, and CRT characteristics. Disease staging was defined according to the 2002 American Joint Committee on Cancer anal cancer staging manual, sixth edition. The pre-treatment evaluation included physical examination, rectal endoscopy with tumour biopsy, transrectal endoscopic ultrasound (EUS), abdominal ultrasound, and SCC antigen dosage. The study was approved by the Institutional Review Board of Tenon Hospital.

### 2.2. Study treatment

All patients started their treatment with CRT. All patients but two underwent a three-dimensional conformal radiation therapy. Intensity-modulated radiation therapy (IMRT) by volumetric modulated arc therapy concerned two patients.

Patients in both centres were treated with radiation therapy plans quite similar to those of anal SCC [4].

A planning computed tomography (CT) scan was required to define target volumes.

In Tenon Hospital, the following volumes were based on the International Commission on Radiation Units and Measurements 50 Report [5]: the gross tumour volume (GTV) was determined on the planning CT scan; the clinical target volume (CTV) was defined as the GTV, anal canal, mesorectum, presacral nodes, bilateral internal, external and primitive iliac nodes, and inguinal nodes; the planning target volume 1 (PTV1) included the CTV plus a safety margin of 10 mm in all directions. In general, the upper beam limit of PTV1 was at the top edge of the sacral vertebral body 1. After 45 Gy, the reduced PTV (PTV2) was limited to the GTV and the centimetric lymph nodes plus a margin of 10 mm in all directions. Treatment was performed with a linear accelerator of at least 6 MV with an isocentric technique. Customised blocks or multileaf settings were used to minimise the radiation dose to the normal tissues and organs at risk (OARs). Total dose on PTV1 was 45 Gy in fractions of 1.8 Gy five times weekly. After a period of rest, the patients received in PTV2 a dose of 15–20 Gy in fractions of 1.8 Gy five times weekly.

The Besançon University Hospital's treatment approach was based on European Organisation for Research and Treatment of Cancer recommendations [6]. For instance, the cranial border of beams was located on to the top of S2. The two sequences of irradiation of 36 Gy and 23.4 Gy were separated by 2 weeks of rest.

Patients received concurrent chemotherapy with different regimens: cisplatin (25 mg/m$^2$ on days 1–4 and 29–32 or 100 mg/m$^2$ on days 1 and 29) and 5-fluorouracil (5FU) (800–1000 mg/m$^2$ on days 1–4 and 29–32) (n = 12); capecitabine (825 mg/m$^2$ bi-daily every day of irradiation) and mitomycin C (10 mg/m$^2$ on days 1 and 50) (n = 4); 5FU (1000 mg/m$^2$ on days 1–4 and 29–32) and mitomycin C (10 mg/m$^2$ on days 1 and 50) (n = 3); mitomycin C (10 mg/m$^2$ on days 1 and 50) and cisplatin (25 mg/m$^2$/week) (n = 1); weekly cisplatin (40 mg/m$^2$/week) (n = 2). One patient did not receive concurrent chemotherapy because of very early stage (T1N0) and severe cardiac comorbidities.

### 2.3. Follow-up

During treatment, patients were evaluated weekly for toxicity by clinical examination. Complete blood count with differential and platelet counts, renal and liver function tests were performed before each cycle of chemotherapy.