

## Abstract

**Background:** From its establishment in 1998, the BOCOC, a not-for-profit organization, has provided non-surgical oncology services for up to 80% of the island's newly diagnosed cancer pts in the context of site specialization.

**Methods:** A retrospective review of the management of pts with NMRC, referred from September 1998 to December 2004 was performed.

**Results:** Forty surgeons referred 117 pts (73 M, 44 F) to the BOCOC. 97% were referred postoperatively, their median age 66 years (range 34-81). The median follow-up 30 months (range 11-79). Preoperative pelvic imaging with CT/MRI and CEA estimation was available in 22/117 and 22/117 pts, respectively. Surgical treatment included an anterior resection in 62 (53%), an abdominoperineal resection in 46 (39%) and a Hartman's procedure in 9 (8%) cases. Distribution of surgical stage was: UICC 0 in 2 (2%), UICC I in 23 (20%), UICC II in 51 (44%) and UICC III in 41 (34%) pts. Involved resection margins were reported in one case, and intra-operative inadvertent perforation in another. The median number of reported lymph nodes was 9 (range 1-31). Adjuvant radio-chemotherapy was offered to 64/117 pts. 14/117 received adjuvant radiotherapy and 41/117, chemotherapy alone. The median interval between surgery and the start of chemotherapy was 52 days (range 4-165) and the median interval between surgery and the start of radiotherapy was 110 days (range 32-241). In 51/68 pts, who received chemotherapy, a total of 219 courses of bolus 5-fluorouracil plus leucovorin (MAYO regimen) were administered. There were 21/62 treatment interruptions due to Gr. III-IV toxicity or patient refusal; 33 pts received no adjuvant treatment (early stage disease or comorbidities/refusal). Three-year disease-free survival (DFS) was 65%, UICC I 100%, UICC II 65%, UICC III 43% (UICC II vs. UICC III p<0.03). Overall 3-year survival was 94% for UICC I 100%, UICC II 93%, UICC III 58% (UICC II vs. UICC III p<0.03). In 30/117 (26%) pts recurrence was recorded during follow-up. Sites of first recurrence were: pelvis in 7 pts (6%), lung in 13, liver in 8, para-aortic nodes in 3 and bones in 1 case. In 3/30 pts salvage surgery was performed.

**Conclusions:** Our survival- and local-control data are consistent with those reported in other series from the MDT approach using adjuvant radio-chemotherapy for "high-risk" rectal cancer. In the future, efforts will be directed towards individualised management in pts with NMRC, in the context of a multidisciplinary approach.

## INTRODUCTION

According to the Cyprus Cancer Registry (CyCR), an average of 53 new cases of adenocarcinoma of the rectum are being diagnosed yearly within the non-occupied part of the island (incidence: 7.5/100.000). Among them, 90% are non-metastatic at diagnosis. During the last decade, management of NMRC has evolved into a complex multidisciplinary field (1). However, a true multidisciplinary team (MDT) culture has not yet been established within the fragmented health-care environment of Cyprus (Cyprus Development Bank). Moreover, modern pre-operative imaging for prediction of the circumferential resection margin (CRM) status (4), selective pre-operative radiotherapy/radiochemotherapy, standardized TME surgery (1), meticulous pathological examination and reporting (5), important components of a high-quality RC care, have not yet been introduced into the routine day-to-day clinical practice in Cyprus. This, combined with the extremely low "caseload" of the 40 general surgeons treating NMRC (6), makes oncological management of this disease in Cyprus a challenging issue. From its establishment in 1998, the BOCOC, a non-profit organization, has provided non-surgical oncology services for up to 80% of the non-occupied part of island's newly diagnosed cancer patients. In March 2000, a policy of sub-specialization was introduced and, since then, NMRC cases have been managed by a radiation oncologist and a medical oncologist dedicated to GI cancer. This is a retrospective audit of management of NMRC patients at the BOCOC over the first six years from its establishment.

## METHODS

Data from 117 pts registered at the BOCOC from September 1998 to June 2004 with the pathological diagnosis of UICC stage 0-III adenocarcinoma of the rectum were evaluated. These patients represent 37% of the expected new cases of NMRC for the examined six-year period (CyCR). During this period, patients referred to the BOCOC with UICC stage II-III RC, age <75 years and an adequate PS were offered the option of adjuvant RTCH, according to the NCI-guidelines. For patients older than 75 years, decision-making for adjuvant treatment was individualized. According to this policy, 82/117 (70%) of all patients with NMRC received adjuvant treatment. Combined modality treatment was offered to 64/117 (55%) of the patients. For RT, routine 3-D planning and a three- or four-field technique were used in all patients. The majority of patients received bolus 5FU chemotherapy according to the NCI guidelines. All patients underwent a follow-up program under the supervision of the two GI-consultants. The starting point of time-event analyses was the date of surgery. Local recurrences and distant metastases were diagnosed histologically or radiologically. For statistical analysis, the Kaplan-Meier method was used for actuarial analysis of local control, disease-free (DFS) and overall survival (OS). Statistical significance was evaluated by the log-rank test.

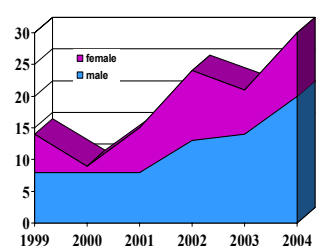
### 1. Patient and disease characteristics n = 117

AGE	median	66
	range	34 - 81
GENDER	male	73 (61%)
	female	44 (39%)
Surgical stage of disease	UICC 0	2 (2%)
	UICC I	23 (20%)
	UICC II	51 (44%)
	UICC III	41 (34%)

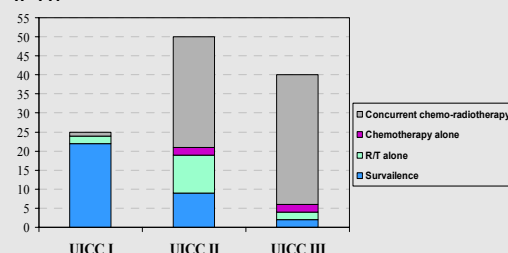
### 2. Initial management

Staging with pelvic CT/MRI	23/117 (20%)
Preoperative CEA available	22/117 (19%)
Type of surgery	
Anterior resection	62 (53%)
Abdominoperineal resection	46 (39%)
Hartman's procedure	9 (8%)
Involved resection margins	1
Inadvertent intra-operative tumor perforation	1
Median number of reported lymph nodes	9 (1-31)

### 3. New referrals per year



### 4. Oncological management according to disease stage n=117



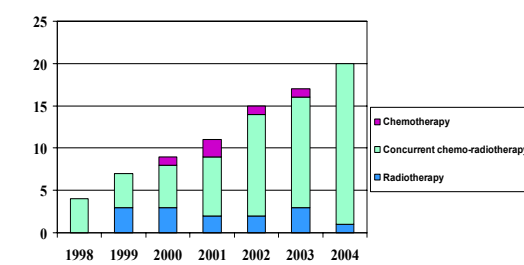
### 5. Radiotherapy (RT)

Total dose	median 50.4 Gy range 7 - 58
Interval surgery - RT	median 110 days range 32 - 241

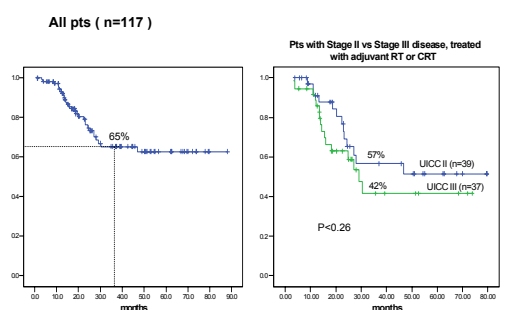
### 6. Chemotherapy

Regimens	"Mayo" : 51 Capecitabine : 6 "De Gramont" : 2 Weekly 5-FU : 5 Oxaliplatin/5FU - MdG : 2
Interval "surgery - chemotherapy"	median 52 days range 4 - 165
Treatment interruption	21 (4 refusal, 17 due to Gr. III - IV toxicity)

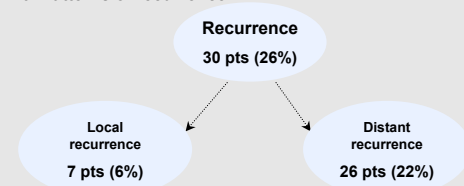
### 7. Adjuvant management n = 82



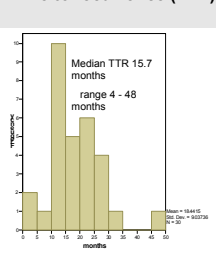
### 8. DISEASE-FREE SURVIVAL



### 10. Patterns of recurrence



### Time to recurrence (TTR)

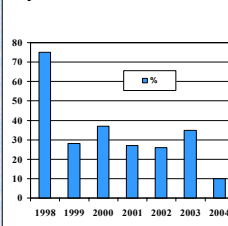


### 11. 7 pts with Local Recurrence

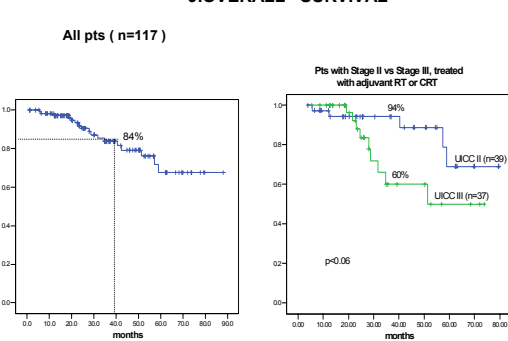
N	Surgery - RT interval, days	Treatment	Dose of RT, Gy	Treatment interruption
1*	37	RT	54	No
2	66	CRT	50	Yes
3	78	CRT	54	Yes
4	92	RT	54	No
5	125	CRT	50	Yes
6	133	CRT	7	Yes
7	-	Ch	-	-

\* Non-radical surgery

### 12. Allocation of pts who had a discontinuation of treatment for any reason



### 9. OVERALL SURVIVAL



## CONCLUSIONS

Over the six-year period under review, a continuous increase in post-operative referrals, utilization of adjuvant RTCH and the rate of patients who completed the adjuvant treatment protocol have been documented. The enhanced interaction between surgeons and oncologists and the sub-specialization effect may have positively influenced these parameters. Oncological outcomes in UICC stage II-III RC are comparable with those reported from other retrospective day-to-day clinical practice audits (8). However, further efforts have to be made towards abandoning the current monolithic approach of upfront surgery followed by adjuvant RTCH, enhance MDT approach, as well as implement modern surgery and quality control assurance programs that are mandatory for optimization of outcomes in NMRC.

## References

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