

RESEARCH ARTICLE

European Colorectal Cancer Management: Implemented as it is or Adapted to our National Specificity?

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Objective: We attempt to evaluate how the European treatment guides are implemented in a clinic hospital in Targu Mures and if those rules could be adopted as they are or must be adapted to our national specificity. **Methods:** For a number of 441 patients included in the study, the electronic prospectively maintained archive of 3rd Surgery was interrogated for: age, preoperative colonoscopy, postoperative colonoscopies, chemo-radiotherapy enrollment, stage of the disease, type of surgery. Local and regional relapses were assessed and their incidence was related to type of surgery. Survival analysis was done in a simplified manner and differentiated for age below and above 75 years. **Results:** Patient's age distribution revealed a deviation to the right compared with a normal distribution with a median off 64.76 ± 11.47 . Colonoscopy was done in only 65 cases, exclusive preoperatively. Chemoradiotherapy was administered in 168 cases, only 12 of them initiated preoperatively. The type of surgery performed was found positively correlate with the stage of the disease. The survival probability for the patients in this study showed a 50% survival rate at 1 year and only 2% at 5 years. **Conclusions:** Passive screening age in CRC should be decreased to 55 years. Stage 3 and 4 of disease for CRC are over 70% of cases, like 20 years ago. Survival rate in CRC is far lower than other studies. Integrated CRC management and European practical guides are still "in wishing" stage.

Keywords: colorectal, cancer survival, management

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Introduction

Since European Union states signed an agreement in 2003 for starting screening programs in colorectal cancer some countries, e.g. Holland, achieved over 35% higher rates in detection of the disease with a significant increasing of early stages detected which have by default a better prognosis and survival rates [1]. In 2012 European Society for Medical Oncology published a "Consensus Guidelines" for management of patients with colon and rectal cancer [2] and in 2013 a series of updated guides [3, 4], concerning all the steps involved in its actual management, from early detection to post procedures surveillance and quality of life assurance.

Oncological principles of surgical resection in colorectal cancer did not change in the last decade; however the techniques evolved for any location toward laparoscopic and robotic surgery. In a meta-analysis involving 4458 cases [5] laparoscopy was found superior to open surgery, reducing the intraoperative blood loss, earlier oral food intake and lower hospital length of stay but with similar long term results. In another study [6], while The United States Association of Colorectal Surgeons did not encourage laparoscopy, in other countries this procedure is found safe and comparable with open surgery regarding relapses and 3 years survival. Laparoscopy was found superior in

high risk patients (in a study over 424 cases [7]) and also in reducing postoperative blood loss, low incidence of intestinal obstruction by adhesions and reduced long term morbidity compared with classic surgery in 1544 cases, without significant changes in local or distant relapses [8].

For 0 and partially 1 stages of colorectal cancer endoscopic resection seems to be the new standard [9]. In a multicentric study [10], 7,378 endoscopic resections compared with 35,116 classical ones were found oncological equivalent for stage 0 and comparable, associated with chemo radiotherapy, for stage 1.

In this study we attempt to evaluate how the European treatment guides are implemented in a clinic hospital in Targu Mures and if those rules could be adopted as they are or must be adapted to our national specificity.

Methods

The prospectively maintained database of 3rd Surgery Clinic was used, in a 10 years period (2004-2013) enrolling 441 patients in study. Additional data for the patients, regarding endoscopies and radio chemotherapy were obtained from Mures County Clinic Hospital Manager Suite database. Survival data, were found both in local databases and from National House of Health Insurance database conducting case by case interrogations using July, 2nd 2014 as end of study's date and obtaining a patient status as "deceased" or "assured" meaning alive.

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For all the patients we collect: age at admission; preoperative colonoscopy date and findings; number, date and findings for postoperative colonoscopies; starting date for radio chemotherapy; type (laparoscopic or open) of surgery and its extent.

Stage of the disease was assessed using pathological reports and the surgery protocols allowing us to accurately distribute the patients in stage 0, 1, 2, 3 or 4.

Local and regional relapses were assessed, excluding non-oncological complications, and correlated with the type of surgery (laparoscopy vs. open surgery).

Survival rates were calculated in a simplified manner for below 3 months, 3, 6 and 12 months, 2, 5 and 10 years using formulas described in Table I.

General statistics, Fischer's exact test and Kaplan-Meier Estimated Survival Rate (KMESR) was performed using Microsoft Excel.

Results

Patients' age distribution (64,76±11,47, Min=26, Max=89) is graphically illustrated in Figure 1.

Colorectal cancer management according to European current guides stratified by stage of the disease is shown in Table II, while the correlation between type of surgery and stage is represented in Figure 2.

Laparoscopic versions for major resections were performed in only 27 cases (6,12%) and the relapses' incidence is shown in Table III.

The survival rates for 7 time intervals are shown in Figure 3 and stratification according to patients' age above or below 75 years is showed in Figure 4.

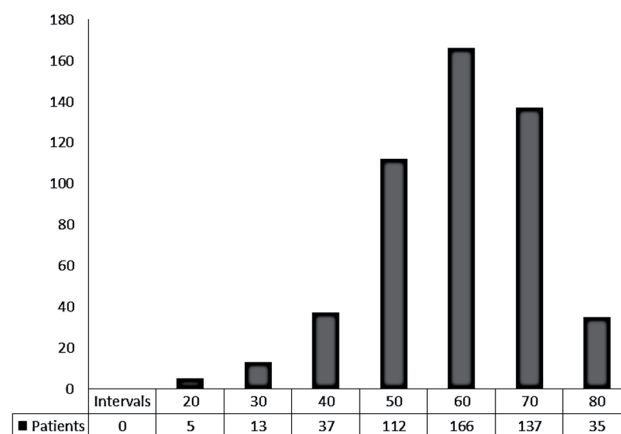


Fig. 1. Patients' age histogram

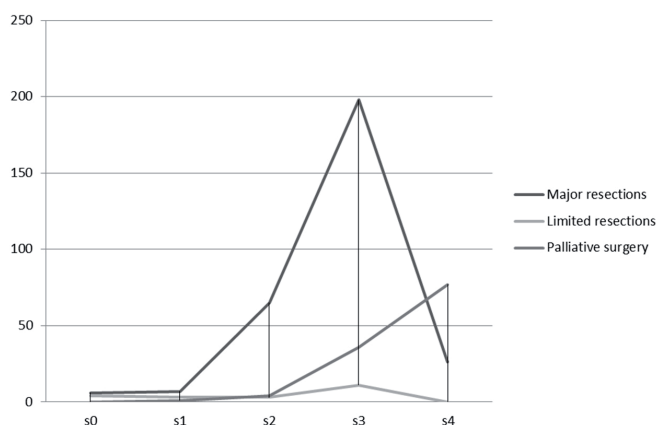


Fig. 2. Correlation between type of surgery and stage of colorectal cancer

Table I. Formulas used for survival calculations

	Months of Survival (MOS)
Patients deceased during hospitalization	$MOS = 12 \cdot \frac{\text{Deceased date} - \text{Admission date}}{365}$
Deceased patients without knowing the date, but having subsequent hospital admissions	$MOS = 12 \cdot \frac{(\text{Date of last discharge} - \text{Date of first admission})}{365}$
Surviving patients at July, 2 nd 2014	$MOS = 12 \cdot \frac{02.07.2014 - \text{Admission date}}{365}$
Deceased patients at July, 2 nd 2014 without subsequent hospital admissions	Those patients were included in the "censored" group

Table II. Colorectal cancer management by stage

	Stage 0	Stage I	Stage II	Stage III	Stage IV	Total
Patients	10	11	72	245	103	441
%	2,27	2,49	16,33	55,56	23,36	100
Preoperative colonoscopy	10	11	32	12	0	65
%	2,27	2,49	7,25	2,72	0	14,73
Preoperative chemo-radiotherapy	0	0	0	9	3	12
%	0	0	0	2,04	0,68	2,72
Postoperative chemo-radiotherapy	0	2	3	86	77	168
%	0	0,43	0,68	19,5	17,46	38,09
Major resections	6	7	65	198	26	302
%	1,36	1,58	14,73	44,89	5,89	68,48
Minor resections	4	3	3	11	0	21
%	0,9	0,68	0,68	2,49	0	4,76
Palliative surgery	0	1	4	36	77	118
%	0	0,22	0,9	8,16	17,46	26,75

Tabel III. Relapses incidence in laparoscopic vs. open surgery

	Open	Laparoscopic	Total	p
Major resections	302	27	329	0,2571
Relapses	21	4	25	
Total	323	31	354	

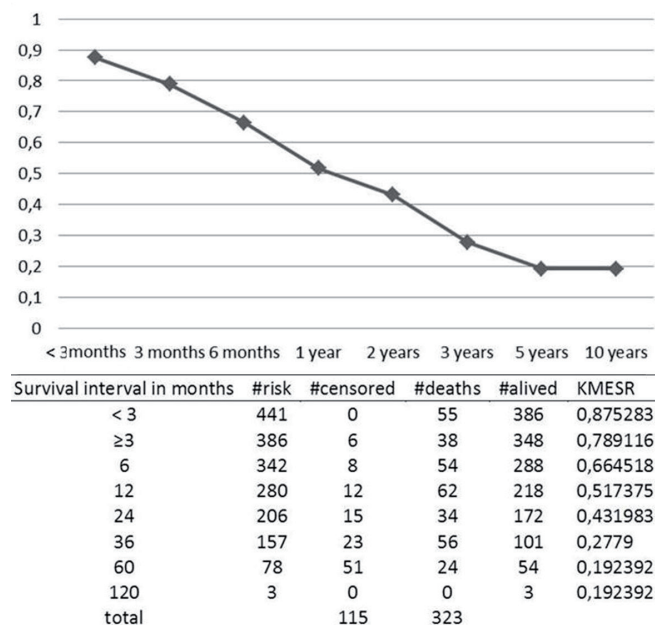


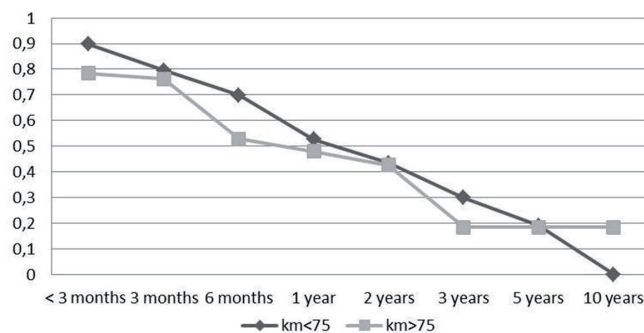
Fig. 3. Kaplan-Meier overall survival curve

Discussion

Patients' age distribution analysis revealed a negative skewness compared with a normal distribution and a positive kurtosis above median values which means a set of values grouped around 65 years even the extreme ages were 28 and 89 years. This is not unusual considering that ages over 60 years are proved to be a risk factor for colorectal cancer and subject for population screening. A peculiar age histogram aspect consists in a 33,78% of patients in 40-60 years interval which means either an increased incidence or a higher rate of detection at that age.

The colorectal cancer management illustrated in Table II reveals serious concern about European guides implementation. The small number of colonoscopies (only 14,76%) could be related to multiple factors (lack of electronically documented colonoscopies prior to 2008, patients from other counties or with colonoscopy performed in private clinics, emergency admissions or emergency surgery for intestinal obstructions developed during bowel preparation prior to colonoscopy, etc.) but remains considerable low. In spite of lacking data about therapeutic response, the chemo-radiotherapy in our study stays better in number of cases enrolled, near 40% of total, knowing that 36% of patients are from other counties ascribed to other oncology clinics.

In our study 78,92% of cases belong to stage III and IV of the disease, a concerning proportion, almost identi-



Survival Months	Age below 75					Age above 75				
	risk	censored	deaths	alived	KMESR	risk	censored	deaths	alived	KMESR
< 3	353	0	36	317	0,89	88	0	19	69	0,78
≥ 3	317	4	36	281	0,79	69	2	2	67	0,76
6	277	6	34	243	0,69	65	2	20	45	0,52
12	237	9	58	179	0,52	43	3	4	39	0,47
24	170	11	30	140	0,43	36	4	4	32	0,42
36	129	23	40	89	0,29	28	0	16	12	0,18
60	66	42	24	42	0,19	12	9	0	12	0,18
120	0	0	0	0	0	3	0	0	3	0,18
total		95	258			20	65			

Fig. 4. Kaplan-Meier survival curve for age below and above 75 years

cal with the one found in a 7 years old paper [11], which means that despite 10 years of technologic breakthrough in medical imaging and increased patients accessibility to colonoscopies, early detection of colorectal cancer is far away from European guides principles.

We found a positive correlation between type of surgery and stage of the disease, similar to European guidelines, but newest laparoscopic techniques are still in small numbers for a pertinent comparable analysis. Relapses after laparoscopy were not found significant different to open surgery.

Survival analysis in this study revealed a shocking 50% survival rate at 1 year and only 2% at 5 years, far away from other studies' results, due to a large number of censored cases, patient's ages and rigid formulas used for calculations. Anyway, survival rate stratification for ages below and above 75 years confirmed that age is a risk factor for colorectal cancer-related mortality.

Conclusions

While CRC patients' age histogram remains centered around 65 years, for passive screening is recommended the 55 years age.

Stage 3 and 4 of disease for CRC overpass 70% of cases, like 20 years ago, despite the increased patient's accessibility for enhanced imagistic and endoscopies.

CRC survival rate in our study is only 2% at 5 years.

Integrated CRC management and European practical guides are still "in wishing" stage.

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