

Age and factors associated with access and time to post-operative adjuvant chemotherapy in colon cancer: a French epidemiological study

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Background: Studies have shown the negative prognostic impact of increased time between colectomy and postoperative adjuvant chemotherapy (AC) in colon cancer (CC). Our aim was to investigate the role of age and non-organizational factors on access and time to AC.

Methods: All adult patients undergoing surgery for stage II or III CC in the “Région Centre-Val de Loire” in 2013, were selected. Time to AC and socio-demographic factors were collected. Logistic regression modeling was used to identify factors associated with access to AC, and a multivariate analysis performed to identify factors associated with time to AC.

Results: Among 404 stage II or III patients who underwent colectomy, 182 (45%; sex ratio 1.5; mean age 67.6 years; range 32–90) received AC. AC patients were younger than those without AC (67.6 vs. 77.9 years) and the difference was even greater for stage III patients (69.0 vs. 82.4). The median time to AC was 48 days, exceeding 42 days in 60% of cases. Living alone, postoperative morbidities, and emergency colectomy were independently associated with increased time to AC. Age and other factors were not associated with delayed AC.

Conclusions: Emergency colectomy, postoperative morbidities, and living alone are associated with increased time to AC. Organizational measures to reduce the time to AC are therefore unlikely to have an impact. In contrast, age is not associated with increased time to AC, but to access to AC. Reasons for omitting AC in older patients requires further study.

Keywords: Colonic neoplasms; adjuvant chemotherapy (AC); geriatrics; epidemiology

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Introduction

Colon cancer (CC) is a major public health problem with 1.4 million cases and more than 600,000 deaths per year worldwide (1). It is the 2nd leading cause of cancer mortality in France (2) and Europe (3), accounting for more than 17 000 deaths each year in France (2). Colectomy remains the cornerstone of treatment and post-operative adjuvant chemotherapy (AC) significantly decreases recurrence and improves survival among patients with high risk stage II (4,5) or stage III colon cancer (5-8). In clinical trials, AC is generally initiated within six to eight weeks after surgery. However, in daily practice, AC is often delayed to more than eight weeks after surgery (9-11) with a negative prognostic impact (9,10,12-16). In addition, older age is associated with fewer AC prescriptions (17,18), despite the fact that chemotherapy is effective in older patients (19-21). Programs in several countries aim to reduce delays and improve access to AC (22,23), but little is known about the associated factors. The objective of our study was to investigate the role of age and other non-organizational factors on access or time to AC in CC patients.

Methods

Study population

We selected cases from our hospital discharge regional database for this multicenter, retrospective, observational, epidemiological study using an algorithm. All adult patients who underwent surgery for stage II or III CC in an authorized health facility for digestive cancer surgery in the “Région Centre-Val de Loire” between January 1 and December 31, 2013, were included. Patients with rectal cancer, a past history of CC, or who received pre-operative chemotherapy were excluded. All data from the medical records were exhaustively included for each health facility.

Data collection

We collected the following data from the patient medical record for each case included in the study: time to AC and likely non-organizational associated factors including age, employment situation, marital status, and medical factors such as the circumstances of diagnosis, emergency or elective surgery, and postoperative morbidities. The study

was approved by the CNIL (the French data protection authorities) and CCTIRS (French Advisory Committee on Information Processing in Material Research in the Field of Health), decision DR-2014-132.

Statistical analyses

The populations with and without AC were compared using the Chi square or Student's test depending on the type of variables. After selection of the relevant variables ($P < 0.1$ by univariate analysis), a multivariate logistic regression model was used to identify factors associated with access to AC.

We studied the time between colectomy and AC for the group that received AC. We excluded the extreme values to calculate the mean time between colectomy and AC, but not for calculating the median. Probable associated non-organizational factors were tested in a univariate linear regression model to select the variables ($P < 0.1$). We then performed a multivariate analysis using a linear regression generalized model (LGM) to identify factors associated with increased time between colectomy and AC. Sex, regional department, and type of health facility (public or private) were included as adjustment variables. Regression coefficients were calculated using SAS 9.3 (SAS Institute).

Results

Population characteristics

Twenty-three of the 24 health facilities of the “Région Centre-Val de Loire” participated in this study from which we identified 914 CC cases from our regional hospital discharge database. Among these, 167 (18%) cases were excluded, mostly due to non-colonic cancer localization ($n=104$) or algorithm selection errors. Among 747 remaining patients, 404 colectomy cases for stage II ($n=240$, 59%) or III ($n=164$, 41%) CC were identified and included in the study (*Figure 1*).

Characteristics of the population are shown in *Table 1*. Stage II CC patients received AC significantly less often than stage III CC patients ($P < 0.0001$). Patients receiving post-op AC were significantly younger than those not receiving AC (mean age of 67.6 *vs.* 77.9 years, $P < 0.0001$). This difference was greater in the stage III only population (mean age of 69 *vs.* 82.4 years, $P < 0.0001$). Patients who did not receive AC were more often not living as a couple and

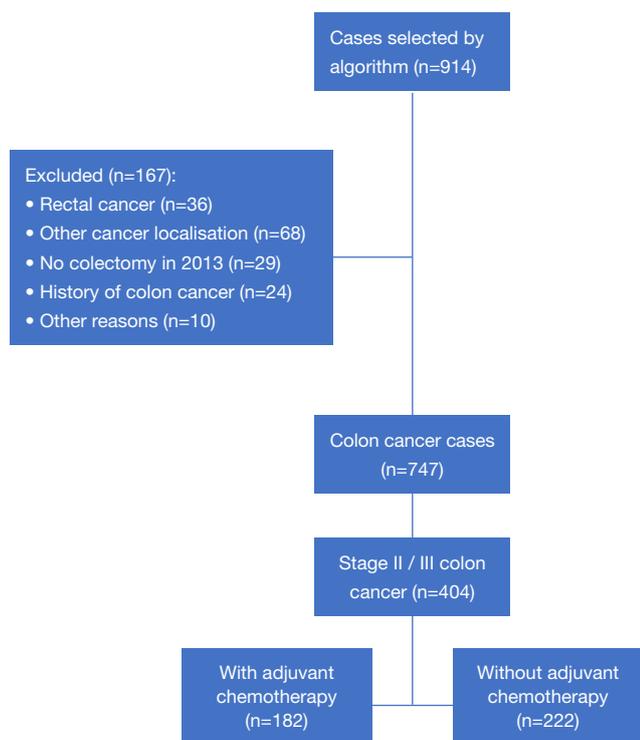


Figure 1 Flow chart of the study population.

were retired.

Factors associated with access to post-operative chemotherapy are shown in *Table 2*. In multivariate analysis, adjusted for the regional departments and type of health facility (public or private), only two factors were associated with not receiving AC: older age ($P < 0.0001$) and cancer stage ($P < 0.0001$).

Time to adjuvant chemotherapy

Among the patients receiving AC, the mean time between colectomy and AC was 48 days ($SD = 14.2$). The time to AC exceeded 42 days in 60% of the cases (*Figure 2*), 56 days in 29%, and 84 days in only 6% (*Table 3*).

There was an association by univariate analysis between time to AC and living as a couple, mode of cancer detection, postoperative morbidities and type of colectomy. Age and colon cancer stage were not associated with increased time to receiving AC (*Table 4*).

Three factors were associated with increased time to AC by multivariate analysis: not living as a couple (+6.7 days, $P = 0.04$), cancer detected during an emergency colectomy

Table 1 Characteristics of the populations with and without adjuvant chemotherapy, "Région Centre-Val de Loire", 2013

Qualitative variable	Total population (n=404)	Population without AC (n=222)	Population with AC (n=182)	P
Gender, n (%)				0.1677
Female	175 (43.3)	103 (46.4)	72 (39.6)	
Male	229 (56.7)	119 (53.6)	110 (60.4)	
Age (years), n (%)				<0.0001
<70	155 (38.4)	52 (23.4)	103 (56.6)	
>70–<80	112 (27.7)	55 (24.8)	57 (31.3)	
>80	137 (33.9)	115 (51.8)	22 (12.1)	
Living as a couple, n (%)				0.0019
No	89 (28.5)	60 (35.9)	29 (20.0)	
Yes	223 (71.5)	107 (64.1)	116 (80.0)	
Professional situation, n (%)				0.0007
Active	40 (15.2)	12 (8.6)	28 (22.8)	
Inactive	11 (4.2)	3 (2.1)	8 (6.5)	
Retired	212 (80.6)	125 (89.3)	87 (70.7)	

Table 1 (continued)

Table 1 (continued)

Qualitative variable	Total population (n=404)	Population without AC (n=222)	Population with AC (n=182)	P
Cancer detection mode, n (%)				0.2417
Clinical signs	313 (78.4)	179 (81.7)	134 (74.4)	
Emergency colectomy	32 (8.0)	15 (6.8)	17 (9.4)	
Organized screening	30 (7.5)	12 (5.5)	18 (10.0)	
Others	24 (6.0)	13 (5.9)	11 (6.1)	
Stage, n (%)				<0.0001
II	240 (59.4)	189 (85.1)	51 (28.0)	
III	164 (40.6)	33 (14.9)	131 (72.0)	
Postoperative morbidities, n (%)				0.1289
No	343 (85.5)	182 (83.1)	161 (88.5)	
Yes	58 (14.5)	37 (16.9)	21 (11.5)	
Colectomy type, n (%)				0.0454
Right	213 (52.7)	131 (59.0)	82 (45.1)	
Left	161 (39.9)	76 (34.2)	85 (46.7)	
Transverse	17 (4.2)	9 (4.1)	8 (4.4)	
Total	13 (3.2)	6 (2.7)	7 (3.8)	
Quantitative variable, mean \pm SD				
Age, years	73.3 \pm 11.7	77.92 \pm 10.6	67.62 \pm 10.48	<0.0001
Age, years (stage III only)	71.7 \pm 11.1	82.39 \pm 9.0	69.0 \pm 9.9	<0.0001

AC, adjuvant chemotherapy.

compared to clinical signs (+7.9 days, $P=0.05$), and the presence of postoperative morbidities (+7.5 days, $P=0.04$) (Table 4).

Discussion

Our study addressed colon cancers eligible for colectomy and focused on patient-dependent factors associated with access and time to AC, two factors that have a prognostic impact. Few studies have focused on these two aspects in the same population.

We included 404 patients who underwent surgery for stage II or III colon cancer, in the “Région Centre-Val de Loire” of France. We selected patients based on a hospital discharge database which covered all colectomies for colon cancer in 23/24 authorized health facilities participating in the study. For each case, access to the medical record made

it possible to collect all available data.

The presence of missing values for socio demographic variables (i.e., living as a couple or not, professional situation, occupational status), due to the retrospective analysis, led to a statistical loss of power but underlines the strength of our significant findings.

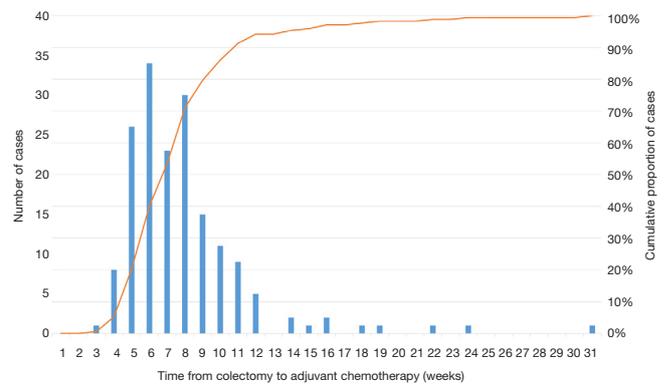
Age was significantly associated with less access to AC ($P<0.0001$), even for stage III colon cancer where AC is strongly recommended in guidelines (24,25). This finding is in accordance with other studies (17,18,26,27). Similarly, the times to AC are similar to those found in the French national study (by the National Cancer Institute), indicating that our regional sample is representative of the CC population.

We found that some patient characteristics are associated with access (age) and time (not living in couple, emergency colectomy and postoperative morbidities) to AC. Measures

Table 2 Multivariate analysis of factors associated with access to adjuvant chemotherapy, “Région Centre-Val de Loire”, 2013

Variables	Multivariable analysis*		
	OR	95% CI	P
Gender			0.93
Female	1.042	0.41–2.66	
Male	1		
Age (years)			<0.0001
<70	1		
≥70–<80	2.891	1.0–8.36	
≥80	20.683	5.67–75.46	
Living as a couple			0.94
No	0.96	0.34–2.68	
Yes	1		
Professional situation			0.28
Active	1		
Inactive	0.788	0.05–11.58	
Retired	2.363	0.72–7.74	
Cancer detection mode			–
Clinical signs	–	–	
Emergency colectomy	–	–	
Organized screening	–	–	
Others	–	–	
Stage			<0.0001
II	36.373	13.42–98.57	
III	1		
Postoperative morbidities			–
No	–	–	
Yes	–	–	
Colectomy type			0.14
Right	1		
Left	0.364	0.15–0.89	
Transverse	0.991	0.11–8.65	
Total	1.075	0.16–7.30	

*, adjusted for regional departments and type of health facility (public or private).

**Figure 2** Number of cases and cumulative proportion according to time to adjuvant chemotherapy (weeks), “Région Centre-Val de Loire”, 2013.**Table 3** Time to adjuvant chemotherapy, “Région Centre-Val de Loire”, 2013

Time	Data
Time to AC (days)	
Mean	48.2
SD	14.2
Median	48
Q1–Q3	38–60
Time to AC exceeding (days)	
42	60%
56	29%
84	6%

AC, adjuvant chemotherapy; Q1, Quartile 1; Q3, Quartile 3.

implemented in several countries to increase access or shorten the time to AC mostly focus on organizational factors which are identified by studying the functioning of each health facility. These measures are unlikely to modify the factors identified in our study, which should be taken into account when evaluating the impact of organizational measures. Finally, age was a factor of that affected access to AC rather than the time to AC. This aspect requires further study and an appropriate oncogeriatric approach.

Table 4 Multivariate analysis of factors associated with time to adjuvant chemotherapy, “Région Centre-Val de Loire”, 2013

Variables	n	Mean	SD	Univariate	Multivariate	
				P	Regression coefficient	P
Intercept					41.9	<0.0001
Gender				0.88		
Female	63	48.4	14.1		-4.2	0.11
Male	99	48.0	14.4		Ref.	
Age (years)				0.17		
<70	93	46.8	14.7		Ref.	
≥70-<80	50	48.7	11.9		0.3	0.92
≥80	19	53.4	16.9		0.6	0.87
Living as a couple				0.05		0.04
No	24	53.5	16.7		6.7	
Yes	104	47.2	13.4		Ref.	
Professional situation				0.74		
Active	27	47.2	16.8			
Inactive	8	51.6	18.0			
Retired	75	47.4	13.8			
Cancer detection mode				0.10		
Clinical signs	118	47.8	13.9		Ref.	
Emergency colectomy	16	56.3	15.7		7.9	0.05
Organized screening	16	48.2	12.2		7.0	0.09
Others	10	43.9	15.0		-4.0	0.40
Stage				0.22		
II	42	50.5	15.5			
III	120	47.4	13.7			
Postoperative morbidities				0.05		0.04
No	144	47.4	14.0		Ref.	
Yes	18	54.3	14.9		7.5	
Colectomy type				0.06		
Right	74	51.1	14.7		1.4	0.82
Left	75	46.3	13.7		-1.6	0.80
Total	7	44.6	10.9		-6.0	0.48
Transverse	6	39.2	11.3		Ref.	

Ref., reference.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the CNIL (the French data protection authorities) and CCTIRS (French Advisory Committee on Information Processing in Material Research in the Field of Health), decision DR-2014-132.

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