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Postoperative mortality risk factors in colorectal cancer: Follow up of a cohort in a specialised unit

José Errasti Alustiza,[a,c,] Baltasar Cermeño Toral,[a] Eugenia Campo Cimarras,[a,c] José Antonio Romeo Ramírez,[a] José Domingo Sardón Ramos,[a] Lorena Reka Mediavilla,[a] Iratxe Arrillaga Alcorta,[a] and Naiara Parraza Díez[b]*

[a]*Servicio de Cirugía General, Hospital Txagorritxu, Vitoria-Gasteiz, Spain*
[b]*Unidad de Investigación de Álava, Hospital Txagorritxu, Vitoria-Gasteiz, Spain*
[c]*Unidad Docente de Medicina de Vitoria, Universidad del País Vasco, Vitoria-Gasteiz, Spain*

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Introduction: The treatment of colorectal cancer (CRC) is usually surgical and involves morbidity-mortality. The aim of this study is to quantify the postoperative mortality in our hospital and to determine their risk factors.

Materials and methods: Prospective observational study from 1996 to 2007 included 1017 patients who underwent surgery for CRC in our hospital. Identification of independent risk factors for postoperative mortality by multivariate analysis.

Results: The mean age was 67.8 years. The surgery was elective in 879 (86.5%) and was considered curative in 878 (86.1%). The postoperative mortality was 3.6% (37 patients), 2.5% in the elective surgery, and 10.9% in the urgent.

The independent risk factors identified were: type of surgery (odds ratio for urgent vs elective = 2.8), American Society of Anesthesiologists (ASA) grade (odds ratio for ASA III–IV vs I–II = 2.4), age (odds ratio for age ≥85 vs ≤74=7.6 and age 75–84 vs ≤74=2.4).

Conclusions: We found a low postoperative mortality, which was mainly associated with age over 75 years, ASA III or IV stages, and urgent surgery.

Factores de riesgo de mortalidad postoperatoria en el cáncer colorrectal: seguimiento de una cohorte en una unidad especializada

Palabras clave:
Neoplasia colorrectal
Cáncer colorrectal

R E S U M E N

Introducción: El tratamiento del cáncer colorrectal (CCR) es habitualmente quirúrgico y conlleva una morbimortalidad. El objetivo de este estudio es cuantificar la mortalidad postoperatoria en nuestro hospital y determinar sus factores de riesgo.

*Author for correspondence.
E-mail address: ose.errastialustiza@osakidetza.net (J. Errasti Alustiza).

Cirugía colorrectal
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Material y método: Estudio prospectivo observacional de los 1.017 pacientes operados en nuestro hospital por CCR desde 1996 hasta 2007. Identificación de factores de riesgo independientes de mortalidad postoperatoria mediante estudio multivariante.
Resultados: La edad media era de 67,8 años. La cirugía se programó en 879 pacientes (86,5%) y se consideró curativa en 878 (86,1%). La mortalidad postoperatoria fue del 3,6% (37 pacientes) (el 2,5% en la cirugía programada y el 10,9% en la cirugía urgente). Los factores de riesgo independientes identificados fueron el tipo de cirugía (odds ratio [OR] para urgente versus programada=2,8), el grado de la American Society of Anesthesiologists (ASA) (OR para ASA III–IV versus ASA I–II=2,4) y la edad (OR para edad ≥85 versus ≤74=7,6 y edad 75–84 versus ≤74=2,4).
Conclusiones: Tenemos una baja mortalidad postoperatoria que se asocia principalmente a una edad mayor de 75 años, a los grados ASA III–IV y a la cirugía urgente.

Introduction

Colorectal cancer (CRC) is the most common cancer in both sexes (excluding skin cancer) and it is estimated that there are 21 000 new patients each year in Spain.[1] Tumour removal remains the most effective treatment to cure CRC. Surgical treatment has improved results with a progressive decrease of morbidity and mortality rates, but the problem still exists.

Knowing the postoperative mortality rate is of great importance as it is one of the quality indicators of the health care process,[2,3] and this allows for the comparison with standards. In the Spanish guidelines[4,5] it is recommended that postoperative mortality be less than 5% for elective surgery and less than 20% for urgent surgery. On the other hand, knowing the risk factors allows us to individually inform each patient regarding their risks.

If we accept that only 80% of the CRCs[6] are operated on and that the postoperative mortality rate is 3%, 500 patients would die each year in our country in the CRC postoperative period, which reveals its great clinical and social importance.

The aim of this study is to quantify the postoperative mortality rate of CRC in our hospital and to determine its risk factors.

Material and methods

Prospective observational study conducted in a hospital of 500 beds, serving a population of 250 000, with undergraduate teaching and training of residents. We included all patients who underwent surgery for CRC in our hospital from January 1996 until December 2007. The 5 surgeons who formed the unit of Coloproctology and residents who rotated through it carried out all the planned surgeries and 70% of the urgent surgeries.

In order to understand our results in the treatment of CRC, in 1996 we created a database that reflected the characteristics of the patient, tumour, surgery, pathology, complementary treatments, and evolution. Data entry was done with the patient's discharge and was updated in outpatients with each follow-up visit. In case of loss of follow-up, patients were contacted by telephone.

Postoperative mortality was considered as that produced until day 30 after surgery, even if they had been discharged from hospital.

Surgery that could not be delayed more than 48 hours was classified as urgent surgery. Elective surgery was defined as that which could be deferred, despite the initial problem being attended urgently, for example, occlusion due to sigmoid neoplasm with initial stent placement and surgery in a second time.

For the assessment of the degree of the American Society of Anesthesiologists (ASA), the physical state scale was used.[7]

Rectal location was determined when the tumour was less than 15 cm from the anal margin. In cases where there were 2 or more tumours and they were located in the colon and in the rectum, it was classified as located in both.

Radical surgery was considered as the total removal of the primary tumour and any possible synchronous metastasis, either in one or 2 times, and in which there was no macroscopic or microscopic residual tumour.

Regarding the resectability, a resectable tumour was defined as one in which complete removal was performed of the primary tumour, but there could still be distant metastases.

The TNM classification system of the American Joint Committee on cancer[8] was used to determine tumour stage.

Postoperative mortality and other risk factors studied were described using univariate analysis.

Subsequently, with the variables that demonstrated a sufficient relationship ($P<.15$) with the dependent variable, we built a multivariate logistic regression model to determine the independent contribution of individual risk factors. We calculated the odds ratio (OR) with a confidence interval (CI) of 95%. The adjustments of the resulting model were assessed using the Hosmer-Lemeshow test. Although the review was conducted on over 1000 patients, the number of events (deaths) was small. Therefore, the ASA grade and TNM stage had to be grouped into 2 categories (ASA: I-II/III-IV; TNM: I-II-III/IV) to facilitate the stability of the estimators obtained. For the same reason, age was grouped into 3 categories (<75/75-84/≥85).

The analysis was performed using SPSS for Windows (version 16.0, Chicago, USA).

Results

During the study period 1017 patients were operated on that demonstrated CRC histologically. The mean age was 67.8 (12) years. Sixty-three percent were men. Thirteen point six percent required urgent surgery (138 patients).

Overall morbidity was 40.6% and was lower in elective surgery (36.9%) than in urgent surgery (64.3%). The type of complication and corresponding percentages are shown in Table 1.

Thirty-seven patients died (3.6%) within 30 days after surgery: 22 (2.5%) after planned surgery and 15 (10.9%) after urgent surgery. One patient died in his home, after discharge, 12 days after surgery, from sudden death. The remaining 36 patients died in hospital. The causes or complications that triggered death are shown in Table 2.

The characteristics of patients, the tumour and the surgery performed with mortality at 30 days and the univariate analysis are shown in Table 3.

Multivariate analysis showed that the variables that maintain an independent association with mortality at 30 days, as shown in Table 4, are found to be age over 75 years (OR=2.4, 95% CI, 1-5.4) and, above all, older than 85 years (OR=7.7, 95% CI, 2.8-21.3), urgent surgery (OR=2.8, 95% CI, 1.3-5.9), and ASA III-IV (OR=2.4, 95% CI, 1.1-5.1). Tumour location, TNM stage, and radical surgery had an association with mortality in the univariate analysis, but this was not maintained after adjusting for other involved factors.

Table 2 – Causes of postoperative mortality

	No. (%)
Dehiscence/anastomotic fistula	13 (35.1)
MOF in urgent surgery[a]	5 (13.5)
Pneumonia	3 (8.1)
Intestinal obstruction	2 (5.4)
Catheter sepsis	2 (5.4)
Aspiration	2 (5.4)
Intra-abdominal abscess	1 (2.7)
Ventral hernia	1 (2.7)
High digestive haemorrhage	1 (2.7)
Urinary sepsis	1 (2.7)
Pulmonary thromboembolism	1 (2.7)
Respiratory insufficiency	1 (2.7)
Heart failure	1 (2.7)
Myocardial infarction	1 (2.7)
Acute pancreatitis	1 (2.7)
Sudden death of unknown cause	1 (2.7)

MOF indicates multiple organ failure.
[a]With death between 1st and 3rd postoperative day.

Discussion

There is a striking discrepancy in mortality rates of different publications, as shown in Table 5. Regional or national revisions in Spain show very high figures, but they give us a more global view, while single-institution studies are usually presented only when they are good or acceptable. Some hospitals with extensive experience have a low postoperative mortality, which varies between 0.8% and 2.3%,[9,10] but others[11-14] refer higher percentages of between 5% and 10.2%. In regional or national audits[6,15-20] the figures range between 4.2% and 9.9%.

Table 1 – Postoperative complications

Complication	%
Wound infection	15.4
Obstruction/ileus	7.8
Dehiscence/anastomotic fistula	6.4
Urinary infection	5.4
Intra-abdominal abscess	3.4
Pneumonia	2.6
Catheter Sepsis	2
Ventral hernia	2
Other sepsis	1.6
DVT/PE	0.9
Haemoperitoneum	0.8
Necrosis/detachment of colostomy	0.7
Other complications	9.5

DVT indicates deep vein thrombosis; PE, pulmonary embolism.

There are few prospective publications with more than 1000 patients regarding postoperative mortality of CRC and its risk factors.[11,18,21] In some, despite being forward looking, the number of patients is relatively small[14,17,22] or they are the results of audits of CRC surgery without analyzing their risk factors.[9,16] Most are retrospective, and thus some risk factors have not been properly analyzed or results are not comparable with ours as they include benign disease,[23,24] only colon cancer,[25] only rectal cancer,[26] or a particular type of treatment. The aim of some publications has been to describe models to individually calculate the probability of postoperative death, such as the Association of Coloproctology of Great Britain and Ireland,[18] the Cleveland Clinic Foundation Colorectal Cancer Model,[10] or CR-POSSUM (colorectal-Physiologic and Operative Severity Score for the Umeration of Mortality).[27]

The data collection methods used in medical literature are different. In some publications[6,20] they are conducted by epidemiologists at central registries, however, in most studies, clinical specialists collect the data.

On the other hand, differences in mortality can also be conditioned by different series with some characteristics that are different and may influence the overall results (some of these features will be discussed later). The proportion of urgent surgery is also very variable, ranging from 3.1% from Fazio et al[10] to 25% of Ferjani et al.[14] The percentage of males is between 51% and 60%, but in the publication of Longo et al[11] it reaches 98%. There are also differences, although less pronounced, in the mean patient age, location, staging, and tumour resectability. Furthermore, the type of hospital, the number of cases per year, and expertise can also influence the results.

It is striking that in Cleveland Clinic[10] series, 24% of deaths occur after discharge. This only occurred in 2.7% of our deaths. This significant disparity may be because we have a

Table 3 – Patient characteristics and univariate analysis of risk factors associated with postoperative mortality

Variables	Patients, No.	Deaths, No.	Mortality, %	Odds ratio (95% confidence interval)	P
Sex					
Male	641	26	4.1	1	
Female	376	11	2.9	0.71 (0.35-1.46)	.355
Age					
≤64	364	6	1.6	1	
65-74	317	7	2.2	1.35 (0.45-4.05)	.596
75-84	286	16	5.6	3.05 (1.45-6.42)	.003
≥85	50	8	16	9.79 (3.85-24.91)	<.001
Type of surgery					
Elective	879	22	2.5	1	
Urgent	138	15	10.9	4.75 (2.40-9.41)	<.001
Preoperative Hb, g/dL					
<10	157	10	6.4	1	
10-15.9	774	25	3.2	0.49 (0.23-1.04)	.064
≥16	72	2	2.8	0.42 (0.10-1.97)	.271
Unknown	14	0	0		
ASA grade					
I-II	694	13	1.9	1	
III	282	20	7.1	4 (1.96-8.16)	<.001
IV	37	4	10.8	6.35 (1.96-20.54)	<.001
Not known	4	0	0		
Location					
Colon	642	31	4.8	1	
Rectum	355	6	1.7	0.34 (0.14-0.82)	.016
Both	20	0	0		
Radicality					
Radical	878	24	2.7	1	
Palliative	139	13	9.4	3.67 (1.82-7.40)	<.001
Resectability					
Resectable	982	33	3.4	1	.126
Unresectable	35	3	8.6	2.6 (0.8-9.0)	.131
TNM stage					
0-I-II	607	16	2.6	1	
III	260	9	3.5	1.32 (0.58-3.04)	.507
IV	150	12	8	3.21 (1.49-6.95)	.003
Overall	1017	37	3.6		

ASA indicates American Society of Anesthesiology; Hb, haemoglobin; TNM, tumour, lymph node, metastasis.

longer postoperative stay, patients with higher mean age and a much higher percentage of urgent surgery. We could not find information specifying the place of death in any other publications.

Age is one of the risk factors that is usually described.[10,15,18,23,28] The OR has been measured for different age groups. Longo et al[11] have done so at intervals of one year and they came up with an OR of 1.032, which seems to have little effect on mortality. However, if we apply this factor to increments of 10 years, it has much more impact. Alves et al[23] divided the patients into 2 groups only, and found that mortality in those over 70 years is multiplied by 2.2. Fazio et al[10] and Tekkis et al[18] created more subgroups, and they come up with an OR around 3.3 and 1.8 for patients aged 65-74 years, 4.8 and 2.8 for patients 75-84 years, and 9.5 and 3.6 for patients over 85 years, with the exception that Tekkis et al[18] show that in patients older than 94 years the mortality is multiplied by 13.3. In our case, the risk is modified slightly between 65 and 74, but is doubled after 75 years and multiplied by 7 after 85. This does not mean that advanced age contraindicates surgery, but it does mean that there should be a great implication to carefully assess if it should be done or not and how on an individual basis, according to the patient and tumour characteristics.

Urgent surgery is another related factor,[11,14,16,18,23] as it approximately triples the mortality rate in most series, like ours. In most publications the percentage of urgent surgery is located between 15% and 20%, but in one case,[10] it only reaches 3%. This low percentage of urgent surgery decreases and masks overall mortality. Therefore, we believe it is important that the results to be assessed should be mortality after planned surgery and mortality after urgent surgery, separately, as standards are usually collected in this manner.

The existence of associated diseases or poor physical condition increases the postoperative morbidity. The physical state can be assessed in a comprehensive and simple manner with the ASA grade, which is clearly associated with postoperative mortality both in the literature[11,10,18] and in

Table 4 – Multivariate analysis of risk factors associated with postoperative mortality

Variables	β Coefficient	Standard error of β	P	Odds ratio (95% confidence interval)
75-84 years	0.86	0.42	.040	2.35 (1.03-5.35)
≥85 years	2.04	0.52	<.001	7.67 (2.76-21.28)
Urgent surgery versus elective surgery	1.03	0.38	.007	2.81 (1.33-5.92)
ASA III-IV versus I-II	0.88	0.38	.021	2.40 (1.14-5.09)
Colon versus rectum	–0.81	0.46	.077	0.44 (0.18-1.09)
Palliative surgery versus radical surgery	–0.96	0.66	.145	0.39 (0.10-1.40)
TMN IV versus I-II-III	0.39	0.68	.571	1.47 (0.39-5.60)
Haemoglobin <10 g/dL	0.16	0.39	.677	1.18 (0.55-2.50)

ASA indicates American Society of Anesthesiology; TNM, tumour, lymph node, metastasis.

Table 5 – Postoperative mortality of colorectal cancer in the medical literature

First author	Year	Area of study	No.	Mortality,% Elective surgery	Urgent surgery	Overall
Mella J[16]	1997	Regional	3221	5.5	21.7	7.6
Semmens JB[6]	2000	Regional	4794	NA	NA	4.2
Staib L[9]	2002	Unicentric	2452	NA	NA	0.8
Tekkis PP[18]	2003	Regional	7374	5.6	14.9	7.5
Tekkis PP[24]	2003	Multicentre[a]	1017	3.2	23.4	7.5
Tekkis PP[27]	2004	Multicentre[a]	6883	2.8	12	5.7
Fazio VW[10]	2004	Unicentric	5034	2.2	6.5	2.3
Pla R[29]	2004	Regional	4443	NA	NA	3.3
Alves A[23]	2005	Multicenter	1421	1.6	11.5	3.4
Nickels TN [20]	2005	Regional	5187	7.1	23.3	9.9
Wong SKC[21]	2005	Multicentre	1217	1.9	6.8	3.4
Villalonga R[13]	2006	Unicentric	749	5.7	13.4	6.4
Ferjani AM[14]	2007	Unicentric	618	6.7	20.2	10.2
Errasti J	2009	Unicentric	1017	2.5	10.9	3.6

NA indicates not available.
[a]Colorectal surgery include benign and malignant processes.

our series. Arguably, ASA grade is fairly non-specific, but is the most simple and universal risk classification system, and therefore it is used in most of the reviews. For Longo,[11] the risk does not increase in grade II, but gradually doubles in the III and IV-V. For Fazio et al[10] and Tekkis et al,[18] mortality doubles from ASA II and up. Different diseases and syndromes have been described that are associated with increased mortality, such as ascites,[11] cerebral-vascular accidents,[11] and neurological comorbidity.[23] Various analytical disorders have also been linked to mortality, such as hypokalaemia,[11] thrombocytopaenia,[11] hyponatraemia, and hypernatremia.[11]

The level of haemoglobin or the haematocrit level as possible risk factors were not analysed in most publications. Fazio et al[10] found that a haematocrit less than 31 is associated with increased mortality. In our experience, patients with haemoglobin below 10g/dL presented higher mortality, but without statistical significance.

Surgery of more advanced tumours presents higher mortality, which is associated with tumour stage,[10,11,16] with the unresectability of the tumour[10,18] or palliative[16] surgery. In our series, all these characteristics were accompanied by a higher percentage of mortality, but after multivariate analysis none of them was a risk factor.

The male sex conditions a higher mortality in some reviews.[25,29] In our study as in others,[10,18] it has a higher percentage of mortality, but without any significant differences.

The colonic location regarding the rectal location is associated with increased mortality in our series and others,[10,18] but without an association in the multivariate analysis.

Other factors have been described such as being overweight[23] and a low socio-cultural status,[17] that we have not taken into account. It is possible that in some specialized centres with excellent results, said results may be conditioned by a low number of homeless patients or low educational level.[11]

There is great amount of medical literature that relates the number of patients attended to by the hospital and the surgeon with the results, which mostly conclude that with a smaller number of patients, there is increased postoperative mortality.[25,30,31] However, Pla et al[29] reviewed the outcome of treatment of different tumours in Catalonia between 1996 and

2000 and found a relationship between caseload and mortality in some tumours but not in the CRC.

As already discussed in the section on materials and methods, although the study involved 1017 patients, the number of events (deaths) was small, which could limit the power of the study to detect any real associations to some of the risk factors. On the other hand, it would have been desirable to not have to add the ASA or TNM categories so that the correspondence with clinical reality were greater.

We conclude that the factors that have had greater impact on the postoperative mortality of our patients were, in order of importance, age over 84 years, the ASA III-IV risk, urgent surgery and age between 75-84 years.

We believe that audits are needed, whether local or regional, to monitor compliance with recommended mortality standards.

Conflict of interest

The authors affirm that they have no conflicts of interest.

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