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(Accepted 19 September 2003)



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BMJ 2003;327:1196-9



The statistical model used by the Association of Coloproctology of Great Britain and Ireland and a list of hospitals participating in data collection appear on [bmj.com](http://bmj.com)

## Operative mortality in colorectal cancer: prospective national study

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### Abstract

**Objective** To develop a mathematical model that will predict the probability of death after surgery for colorectal cancer.

**Design** Descriptive study using routinely collected clinical data.

**Data source** The database of the Association of Coloproctology of Great Britain and Ireland (ACPGBI), encompassing 8077 patients with a new diagnosis of colorectal cancer in 73 hospitals during a 12 month period.

**Statistical analysis** A three level hierarchical logistic regression model was used to identify independent predictors of operative mortality. The model was developed on 60% of the patient population and its validity tested on the remaining 40%.

**Results** Overall postoperative mortality was 7.5% (95% confidence interval 6.9% to 8.1%). Independent predictors of death were age, American Society of Anesthesiology (ASA) grade, Dukes's stage, urgency of the operation, and cancer excision. When tested the predictive model showed good discrimination (area under the receiver operating characteristic curve = 0.775) and calibration (comparison of observed with expected mortality across different procedures; Hosmer-Lemeshow statistic = 6.34, 8 df, P = 0.610).

**Conclusions** Clinicians can predict postoperative death by using a simple numerical table derived from the statistical model of the ACPGBI. The model can be used in everyday practice for preoperative counselling of patients and their carers as a part of multidisciplinary care. It may also be used to compare

the outcomes between multidisciplinary teams for colorectal cancer.

### Introduction

Surgeons and the units in which they work are now clearly accountable for clinical outcomes.<sup>1</sup> Consent to surgery cannot be truly informed unless operative risk is estimated by considering the patient's comorbid condition, extent of disease, and complexity of the proposed treatment. Patients and carers may then make decisions with greater awareness of the risks involved.

We describe the development of a dedicated model for colorectal cancer that estimates the operative risk for individual patients while providing an example of the general problem of quantifying surgical risk.

### Data and methods

#### Data sources

The colorectal cancer study of the Association of Coloproctology of Great Britain and Ireland (ACPGBI) was conducted prospectively in 73 hospitals. Data were collected using the standardised ACPGBI dataset<sup>2</sup> or equivalent. The contributing hospitals reported a total of 8077 new cases of colorectal cancer over a 12 month period between 1 April 1999 and 31 March 2001.

We excluded patients with a diagnosis of colorectal cancer who did not undergo surgery and patients of whom only the name and demographic details were recorded on the database, without information on outcomes or risk factors.

#### Study end point and risk factors

The primary outcome was operative mortality, defined as death occurring within 30 days of an operative pro-

cedure, from whatever cause, occurring either in hospital or after discharge from hospital. The risk factors related to patients and procedures in the ACPGBI database included age; sex; American Society of Anesthesiology (ASA) grade<sup>3</sup>; cancer site; surgical procedure<sup>4</sup>; operative urgency classified as emergency, urgent, scheduled, or elective<sup>5</sup>; cancer staging<sup>6</sup>; timing of surgery during a 24 hour period; cancer excision; and annual case volume.

### Statistical analysis

We used univariate logistic regression to identify risk factors related to the operative mortality within 30 days (see [bmj.com](#)).

**ACPGBI colorectal cancer model**—We used multilevel logistic regression analysis to adjust for multiple risk factors, their interactions, and the clustering of adverse outcomes in hospitals (see appendix 1 on [bmj.com](#)). We used the coefficients derived from the multivariate analysis as weights in the derivation of the ACPGBI colorectal cancer score (table 1).

**Model validation**—We validated the model internally by dividing the data into two distinct sets. We developed the model on 60% of the study population, selected randomly, and the remaining 40% of patients used for testing the model. We used the Hosmer-Lemeshow statistic<sup>7</sup> to evaluate the performance of the ACPGBI colorectal cancer model to assess calibration or goodness of fit (the ability of the model to assign the correct probabilities of outcome to individual patients); a high P value indicates good model fit. Model discrimination refers to the ability of the model to assign higher probabilities of death to patients who actually die than to patients who live: we measured this by the area under the receiver operator characteristic curve or c-index. Values ranging from 0.7 to 0.8 represent reasonable discrimination, and values exceeding 0.8 represent good discrimination.<sup>8</sup>

## Results

Altogether, 7374 (91.3%) of 8077 patients presenting with colorectal cancer had no exclusion criteria. We excluded from the analysis 499 (6.2%) patients who did not have surgical treatment and 204 (2.5%) patients whose records were incomplete. Operated cases were submitted by 73 hospitals scattered across all 11 geographical regions in the United Kingdom. A total of 4491 patients (60.9%) had complete data for the risk factors included in the final ACPGBI model. We found no evidence of systematic under-reporting of risk factors, and missing data were distributed evenly among hospitals, with no significant differences in outcomes between missing and non-missing data. Unadjusted postoperative mortality was 7.5% (range 2-14.5%). The patients' demographic characteristics, 30 day postoperative mortality, unifactorial and multifactorial analysis are shown on [bmj.com](#).

Increasing age was found to be associated with a higher operative mortality among the four ASA grades; adjusted odds ratio of 1.53 per 10 years' increase in age (95% confidence interval 1.36 to 1.73). Operations performed on patients with ASA grade II, III, and IV were associated with a 2.0-fold (1.2 to 3.2), 5.3-fold (3.2 to 8.5), and 15.8-fold (9.2 to 27.0) increase

The colorectal cancer model of the Association of Coloproctology of Great Britain and Ireland (ACPGBI) and conversion chart of ACPGBI score to predicted 30 day operative mortality for patients undergoing surgery for colorectal cancer

	ACPGBI colorectal cancer model		Conversion chart	
	Risk factor	Score	ACPGBI colorectal cancer score	Predicted mortality %
Age group	<65	0	0	0.8
	65-74	0.7	0.1-0.4	0.9-1.1
	75-84	1.1	0.5-0.8	1.3-1.7
	85-84	1.3	0.9-1.2	1.9-2.5
	95+	2.6	1.3-1.6	2.8-3.7
Cancer resected	ASA* I	0	1.7-2.0	4.1-5.4
	ASA II	0.8	2.1-2.4	6.0-7.9
	ASA III	1.6	2.5-2.8	8.6-11.3
	ASA IV-V	2.5	2.9-3.2	12.3-16.0
Cancer not resected	ASA I	1.7	3.3-3.6	17.4-22.1
	ASA II	1.8	3.7-4.0	23.9-29.8
	ASA III	2.1	4.1-4.4	31.9-38.7
	ASA IV-V	2.4	4.5-4.8	41.1-48.5
Cancer staging	Dukes's A	0	4.9-5.2	51.0-58.4
	Dukes's B	0	5.3-5.6	60.8-67.7
	Dukes's C	0.2	5.7-6.0	69.9-75.8
	Dukes's D or any metastases	0.6	6.1-6.4	77.6-82.4
Operative urgency	Elective	0	6.5-6.8	83.8-87.4
	Urgent	0.8		
	Emergency	1.1		

The probability of death  $R$  can be calculated by using the ACPGBI equation as follows:  $\ln(R/1-R) = -4.859 + (\text{ACPGBI colorectal cancer score})$

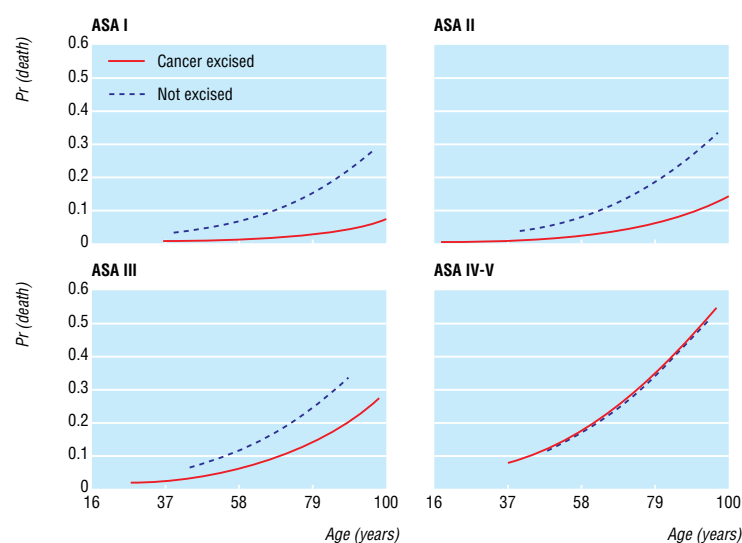
\*American Society of Anesthesiology grade.

in operative mortality compared with patients with ASA grade I, after adjusting for age and hospital effect.

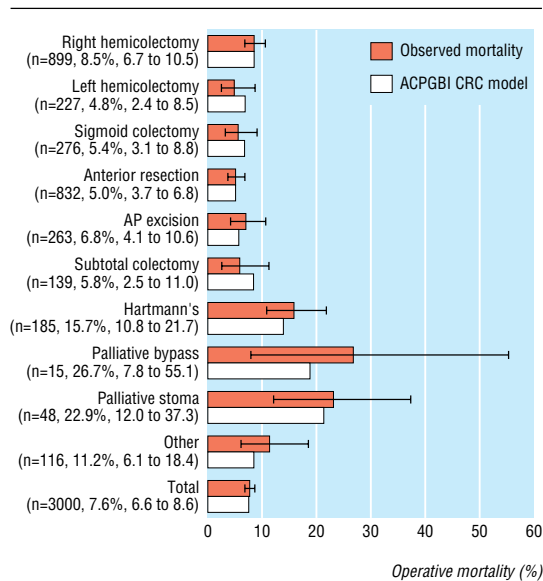
Increasing ASA grade was associated with a higher operative mortality, but this effect differed according to whether or not patients had their cancer resected (fig 1). Cancer excision seemed to confer an advantage in terms of predicted outcome in three of the four ASA categories. This effect diminished with increasing ASA grade, and for patients with ASA grade IV-V the two lines overlapped, indicating a similar outcome between patients who underwent cancer resection and those who did not.

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**Fig 1** Variation of operative mortality by age, ASA grade, and cancer resection. The regression lines have been adjusted for age, ASA, and the interaction term ASA×cancer resection



**Fig 2** Comparison of observed and predicted 30 day operative mortality by type of procedure on the validation set of 3000 cases (Hosmer-Lemeshow statistic 6.34, 8 df,  $P=0.610$ ). For each procedure the number of cases, the observed 30 day operative mortality (%), and its 95% confidence intervals are displayed

*Development of the ACPGBI colorectal cancer model*—On multivariate analysis, the patient's age, ASA grade, urgency of procedure, Dukes's stage, cancer excision, and the product of ASA grade and cancer excision (interaction term) were found to be independent predictors of outcome. The derived ACPGBI colorectal cancer model is a simple additive score and results in a corresponding probability of 30 day operative mortality (table 1).

*Model performance*—The model fitted the data well (Hosmer-Lemeshow statistic for development set:  $P=0.649$ ; validation set:  $P=0.640$ ). The area under the receiver operating characteristic curve was 0.775 (95% confidence interval 0.744 to 0.806).

On subgroup analysis, the predicted mortality for various types of operations for the validation set ( $n=3000$ ), as calculated by the ACPGBI colorectal cancer model, was well within the confidence limits of the observed outcome as shown in figure 2 (Hosmer-Lemeshow statistic:  $P=0.610$ ). Observed and expected mortality did not show any significant differences among the strata of age, ASA grade, Dukes's stage, and urgency of the procedure.

## Discussion

We used 30 day mortality as an indirect measure of the quality of care. In the future the need might arise to include a combination of in-hospital and 30 day operative mortality. It is important to note that if surgeons are simply governed by achieving the lowest death rates they may fail to understand that well informed patients may trade off a short term risk in exchange for "cancer cure."<sup>9</sup> Patients with advanced cancers may not be suitable for cancer resection as the risks of resectional surgery outweigh the benefits of a simpler and possibly safer palliative operation. This is particularly true for obstructed, metastatic cancers of the large bowel, where

palliation with colonic stenting offers an alternative definitive treatment to potentially high risk surgery.

## Validity of the data

An essential prerequisite for the evaluation of healthcare outcomes is the provision of comprehensive, accurate, clinically valid, and reliable information. Although currently the quality of the data may be limited by the observational nature of this study, implementation of such a system should increase awareness of the minimum required data, with subsequent improvement in quality. The study was based on data that we had carefully and voluntarily collected from hospitals throughout the United Kingdom. Since these hospitals were self selected, inferences cannot be made about how representative the outcomes are for the overall population. Although the model was internally validated for the study population, it would require external validation by testing the model on further prospective series in different hospitals.

## Usefulness of the ACPGBI colorectal cancer model and future developments

In the model adjustment was made for age, ASA grade, Dukes's stage, urgency of the procedure, and cancer excision, which are well established, independent, prognostic factors in colorectal cancer.<sup>10</sup> In addition, we introduced an interaction term, which was clinically relevant and clearly improved performance of the model. Although ASA grade is simple to use and has been incorporated by other predictive indices,<sup>11</sup> it is open to subjectivity and manipulation. In future years the ACPGBI dataset can be augmented with other measures of patients' comorbidity, such as the risk factors from the POSSUM physiological score<sup>12</sup> or from the Veterans Affairs surgical risk model.<sup>13</sup> The drawback of using specialised investigations such as albumin, prealbumin, or liver function tests is that, although they may be readily, prospectively, collected in elective situations, in the emergency setting data collection and score generation may be incomplete and lead to incorrect assessment of operative risk.<sup>14</sup> Further work is therefore required to evaluate the accuracy, reliability and cost involved in collecting such data in addition to the ASA grade. Although POSSUM and p-POSSUM systems have been widely applied in general and colorectal surgery,<sup>15 16</sup> disease specific models have been shown to outperform models designed to predict over a range of different conditions. The weights assigned to clinical variables depend on the specific disease context, such as colorectal cancer.<sup>17</sup>

## Conclusions

Clinicians can predict postoperative death in patients with colorectal cancer by using a simple numerical table derived from the statistical model of the ACPGBI, which may provide patients and carers with an estimated numerical probability of survival from surgery as part of the decision making process in the perioperative setting. Our study represents a nationwide attempt to provide accurate risk adjusted outcomes in colorectal cancer care. Review of the observed performance statistics (validity and accuracy) of the model indicates that this was adequate for the prediction of risk to individual patients. A further use for the ACPGBI model might be to compare the

### What is already known on this topic

Risk factors associated with postoperative mortality in colorectal cancer surgery are well established

Predictive models are available for surgical patients in general but are not applicable for predicting individual risk and analysis of subgroups in patients with colorectal cancer

### What this study adds

A dedicated model has been developed to predict operative mortality for patients undergoing surgery for colorectal cancer

This modified model is presented in a format that is suitable for frontline clinicians

results of treatment between units. However, before such comparative studies can be undertaken it will be essential to ensure inclusion of all patients and to have robust methods of data validation.

The research on which this article is based was funded by the Hue Falwasser fellowship of the Royal College of Surgeons of England. The authors thank all the consultants who contributed patients to the study and the data collection officers, managers, and audit facilitators for their invaluable assistance. For a list of hospitals that took part in data collection for the ACPGBI study see [bmj.com](http://bmj.com)

Contributors: see [bmj.com](http://bmj.com)

Funding: PPT is funded by the Hue Falwasser research fellowship of the Royal College of Surgeons of England.

Competing interests: None declared.

Ethical approval: The study was approved by the multicentre ethics research committee for Wales, 10 January 2001.

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(Accepted 18 August 2003)

## RESEARCH POINTERS

# The thrifty phenotype hypothesis and hearing problems

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While looking for solutions to sensorineural hearing loss (SNHL) induced by age or noise, a serious incurable health problem, we became interested in the thrifty phenotype hypothesis because diseases related to this hypothesis are sometimes those linked to SNHL.<sup>1</sup> According to the hypothesis, events during fetal life, such as malnutrition, may cause disease in adulthood. The malnourished fetus makes metabolic adaptations, which may become permanently programmed, persisting throughout life and causing disease later in life. For example, cardiovascular disease,<sup>2</sup> hypertension, obesity, and hypercholesterolaemia are related to reduced fetal growth as reflected by a reduced birth size and to SNHL.

The mechanisms behind the thrifty phenotype hypothesis are unclear, but links to insulin-like growth factor I (IGF-I) have been suggested. During

development, IGF-I is crucial for several organs. This includes the size of the cochlea and auditory neurones; the innervation of the auditory sensory cells; and the postnatal survival, differentiation, and maturation of auditory ganglion cells.<sup>3</sup> Intrauterine growth retarded newborn babies and malnourished pregnancies have lower concentrations of IGF-I. Also, in Turner syndrome SNHL is associated with short stature and lower concentrations of IGF-I.<sup>4</sup> To test the thrifty phenotype hypothesis on SNHL, we reanalysed data from two previous samples, assuming that people who are short in stature are over-represented among non-syndromic individuals with SNHL.

## Participants, methods, and results

We assessed hearing with standard audiometry in 479 men aged 20 to 64, who were exposed to noise in their jobs, and 500 randomly selected 18 year old

**Shortness indicates that hearing problems in adulthood may be programmed at birth**

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*BMJ* 2003;327:1199-200