Postoperative Complications and Mortality after Surgery for Gastric Cancer

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Complication rates and postoperative mortality were studied in 1010 consecutive patients entered into the Norwegian Stomach Cancer Trial. Twenty-eight per cent of the patients had one or more complications (31% of the men and 21% of the women). General complications (pneumonia, thromboembolic, and cardiac) were most frequent. The postoperative mortality rate for resected patients was 8.3% (63 of 763). Complication and mortality rates were highest for proximal resections (52% and 16%) followed by total gastrectomy (38% and 8%), subtotal resection (28% and 10%), and distal resection (19% and 7%). By logistic regression analysis it was found that age, sex, operative procedure, prophylactic antibiotics, and splenectomy were significantly related to postoperative complications. The odds ratio for complication for men *versus* women was 1.75: for no antibiotics *versus* antibiotic prophylaxis it was 2.5. Relative to distal resection the odds ratio for complications after subtotal resection was 2.2, for total gastrectomy was 3.9, and for proximal resection was 7.6. Age and sex were the only factors that affected operative mortality. The odds ratio for mortality for men *versus* women was 2.3. The odds ratio for operative mortality was 2.2 when the age of the patient increased with 10 years.

DESPITE IMPROVEMENTS IN diagnostics, pre-, intra-, and postoperative care and surgical technique, the complication rate after surgery for gastric malignancy has virtually remained unchanged during the last two decades.[1-4] Complication rates of 20–40% and hospital mortality rates of 10–33% are commonly reported in Western series,[1,5-7] which contrast a mortality rate of 2–3% reported from Japan.[8,9] It seems that extensive procedures, such as total gastrectomy, carry a higher complication rate than partial resections.[1,3-5] Consequently, the extensive operation must be followed by an improved long-term survival advantage to be justified.

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Some studies indicate that a survival advantage for extensive gastric resections as compared to less radical procedures may be achieved if the high postoperative morbidity and mortality rates after the former operation can be reduced.[10,11] A reduction in the complication rate may be attained if factors related to complications are identified. So far, little is known about clinical and operative factors related to postoperative morbidity and mortality.

The purpose of this paper was to analyze predisposing factors related to postoperative complications and mortality after gastric surgery for cancer. Further, it was our intention to study a possible relation between complication rates and hospital level to identify the effect of level of care on morbidity and mortality.

Patients and Methods

The Norwegian Stomach Cancer Trial is organized as a prospective observational study with 51 surgical units participating. The patient accrual started September 1, 1982. By December 31, 1984, 1165 patients (705 men and 460 women) had been included. These patients represent 54% of all patients with stomach cancer registered by the Cancer Registry of Norway during the same period. The participating hospitals submitted information on each patient recorded on data sheets to the study headquarters at the University Hospital in Bergen for punching and subsequent analyses.

Of the 1165 patients entered, 1010 (87%; 608 men and 402 women) underwent surgery and 763 patients (65%) had a resection.

TABLE 1. *Complications for 1010 Patients Operated On for Stomach Cancer*

	No. of Complications*	Per cent of Patients Operated On
Intestinal obstruction	15	1
Postoperative hemorrhage	25	2
Anastomotic insufficiency†	41	4
Intra-abdominal infection	37	4
Wound infection	37	4
Wound dehiscence	12	1
Septicemia	42	4
General complications‡	177	18
No complications	722	72

* Some patients had more than one complication.
† Demonstrated on routine x-ray studies at 5–7 days after operation.
‡ Cardiac, pulmonary, thromboembolism, etc.

Pre- and intraoperative variables that may be related to postoperative complications and mortality were cross-tabulated and analyzed with chi-square statistics. The following factors were considered: age (18–59, 60–69, 70–79, 80–91 years), sex, hospital level (University, County, local), preoperative weight loss (≤5 kp, ≥6 kp), operative procedure, operative evaluation (curative *vs.* palliative resection), splenectomy, prophylactic antibiotics, anastomotic technique (stapler *vs.* hand-sutured), and stage of the disease (TNM classification[12]).

Postoperative mortality was defined as all deaths related to postoperative complications as specified on the registration forms, irrespective of whether the patients died before or after 30 days after operation.

To further analyze interactions between variables related to complications and mortality, we performed a backward stepwise logistic regression analysis,[13] taking into account all possible second-order interactions. By this approach we could study the effect on the dependent variable (*i.e.*, complications and mortality) of one particular variable, whereas all other variables were held constant. Separate analyses were performed with complications and mortality as dependent variables, respectively. The logistic regression analysis was restricted to patients having a resection (763 patients). In the logistic regression analysis, age was included as a continuous variable.

The final regression model should fulfill the following three requirements: (1) the model should fit the ob-

TABLE 2. *Complications and Mortality by Type of Operation for 1010 Patients Treated for Stomach Cancer*

	Complications	Mortality
	No. of Patients (%)	No. of Patients (%)
Total gastrectomy (N = 350)	134 (38)	27 (8)
Subtotal gastrectomy (N = 151)	42 (28)	15 (10)
Proximal resection (N = 31)	16 (52)	5 (16)
Distal resection (N = 231)	43 (19)	16 (7)
Gastroenterostomy (N = 72)	16 (22)	7 (10)
Fistulas, tubes, etc. (N = 17)	4 (24)	1 (6)
Explorative laparotomy (N = 158)	21 (13)	5 (3)

TABLE 3. *Complications and Operative Mortality by Sex, Age, Preoperative Weight Loss, Prophylactic Antibiotics, Splenectomy, Anastomotic Technique, and Hospital Level for 763 Patients Resected for Stomach Cancer*

	Complication	Mortality
	No. of Patients (%)	No. of Patients (%)
Sex		
Men	163/461 (35.4)	45/463 (9.7)
Women	72/298 (24.2)	18/299 (6.0)
Not stated	4	2
Age		
≤59 years	27/146 (18.5)	2/145 (1.4)
≤69 years	74/219 (33.8)	12/221 (5.4)
≤79 years	98/288 (34.0)	33/289 (11.4)
≥80 years	36/106 (34.0)	16/107 (15.0)
Not stated	4	1
Weight loss		
≤5 kg	119/361 (33.0)	24/362 (6.6)
≥6 kg	69/218 (31.7)	22/219 (10.0)
Not stated	184	182
Prophylactic antibiotics		
Yes	160/550 (29.1)	43/554 (7.8)
No	68/187 (36.4)	18/186 (9.7)
Not stated	26	23
Anastomotic technique		
Staplers	113/311 (36.3)	26/310 (8.4)
Hand sutures	119/440 (27.0)	36/442 (8.1)
Not stated	12	11
Splenectomy		
Yes	109/260 (41.9)	22/261 (8.4)
No	125/493 (25.4)	39/495 (7.9)
Not stated	10	7
Hospital level		
University	110/234 (34.0)	18/326 (5.5)
County	33/165 (20.0)	13/165 (7.9)
Local	91/269 (33.8)	32/270 (11.9)
Not stated	5	2
Stage of disease (TNM)		
I	24/99 (24.2)	3/98 (3.1)
II	68/185 (36.8)	17/185 (9.2)
III	107/340 (31.5)	33/344 (9.6)
IV	23/94 (24.5)	4/94 (4.3)
Not stated	45	42

TABLE 4. *P Values Revealed by Cross-tabulations and Statistical Analysis (Chi-Square Statistics)*

	Complication (p value)	Mortality (p value)
Age	0.004	0.001
Sex	0.001	0.07
Hospital group	0.003	0.02
Preoperative weight loss	0.74	0.14
Surgical procedure	0.001	0.29
Splenectomy	0.001	0.79
Prophylactic antibiotics	0.06	0.41
Anastomotic technique	0.007	0.91
Operative evaluation	0.74	0.89
Stage of disease (TNM)	0.08	0.08

TABLE 5. *Odds Ratios for Postoperative Complications as Estimated from the Logistic Regression Analysis*

Variable Categories	Odds Ratios	p Value	95% CI
Sex		0.002	
Women	1		
Men	1.75		1.22–2.52
Age		0.0001	
x	1		
x + 10	1.59		1.31–1.92
Surgical procedure		0.0001	
Distal resection	1		
Subtotal resection	2.24		1.32–3.79
Total gastrectomy	3.74		2.18–6.42
Proximal resection	7.23		3.00–17.42
Prophylactic antibotics		0.0001	
Given	1		
Not given	2.42		1.59–3.69
Concomittant splenectomy		0.01	
No	1		
Yes	1.73		1.13–2.65

served data adequately, *i.e.*, give a Hosmer's test of fit with $p > 0.05$[14]; (2) to adjust for multiple significance testing, a significance level for each variable of 0.01 rather than 0.05 was applied as a stopping criterion,[15] thus reducing the overall probability of Type I error to an acceptable level; (3) the final model should explain the effect of individual variables on complications or mortality in the simplest way (most parsimonious model[16]).

The computations were performed by the BMDP[14] statistical program package implemented on the Univac 1100 computer at the University of Bergen.

Results

Overall Results

The number of complications encountered in the 1010 patients operated on are given in Table 1. The overall complication rate was 28%: 31% for men and 21% for women. General complications (pulmonary, thromboembolic, and cardiac) were most frequently found.

Postoperative complications and mortality according to operative procedure are given in Table 2. The complication rate was highest for proximal resection (52%) followed by total gastrectomy (38%), subtotal resection (28%), and distal resection (19%). The operative mortality for all resected patients was 8.3% (63 of 763): 16% for patients having a proximal resection, 10% following subtotal resection, 8% for total gastrectomy, and 7% for distal resection.

Resected Patients

Patients resected for cure had a complication rate of 30.9% (177 of 573) and a mortality rate of 8.0% (46 of 574) *versus* 31.3% (57 of 182) and 9.2% (17 of 184) for patients having a palliative resection (no significant differences). The tumor stage (TNM classification) did not affect complication and mortality rates (Tables 3 and 4).

Cross-tabulations between postoperative complications and other pre- and intraoperative variables revealed statistically significant associations between the dependent variable complications and age, sex, hospital level, operative procedure, splenectomy, and anasto-

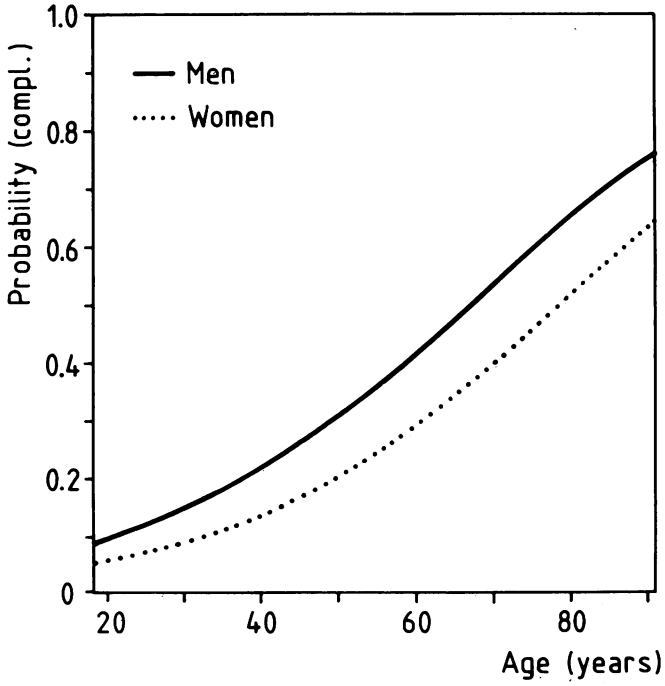

FIG. 1. Probability of postoperative complication for men and women according to age.

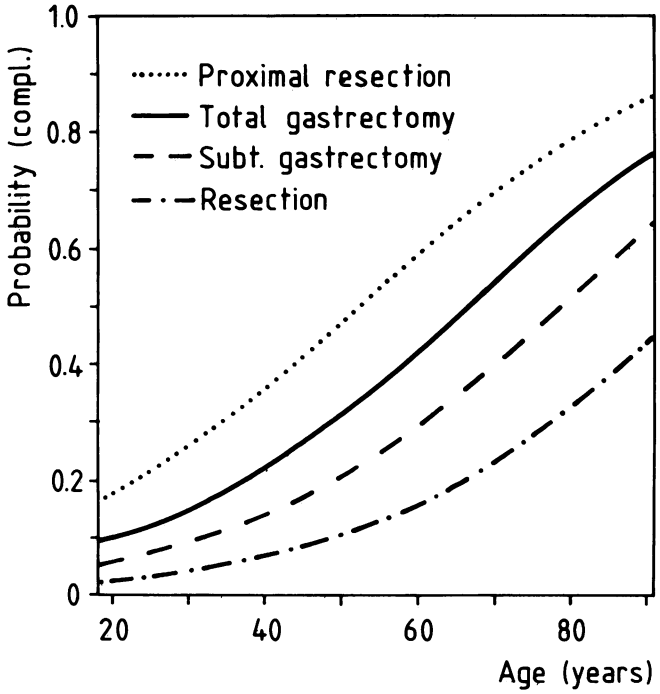

FIG. 2. Probability of complication after various operative procedures *versus* age.

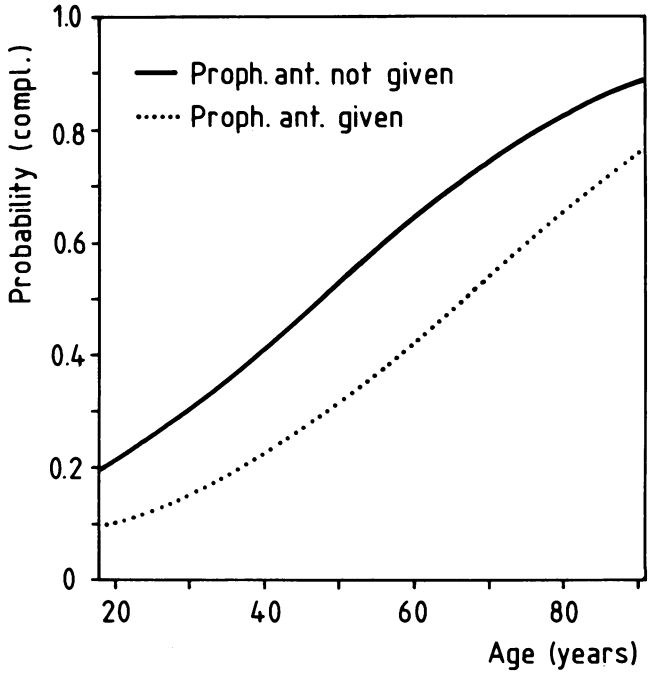

FIG. 4. Probability of complication related to administration of prophylactic antibiotics and according to age.

motic technique. Further analyses revealed that age and hospital group were related to operative mortality (Tables 3 and 4).

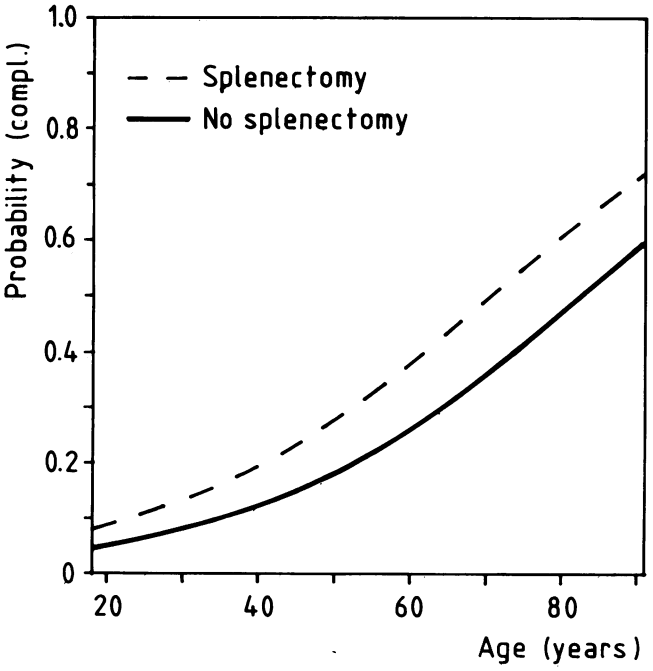

FIG. 3. Probability of complication after concomitant splenectomy *versus* age.

The final logistic regression model fitted the data well ($p = 0.33$ for goodness of fit). By this analysis we found that complications were significantly influenced by sex, age, operative procedure, prophylactic antibiotics, and splenectomy. Preoperative weight loss, anastomotic technique, operative evaluation, and stage of disease were not associated with complication rate, whereas hospital level was of borderline significance. The odds ratios with 95% confidence intervals and p values are given in Table 5. Men had a higher complication rate than women (estimated odds ratio of 1.75). For operative procedures, the lowest complication risk was found after distal resection, whereas proximal resection carried the highest odds ratio, *i.e.*, 7.2 times higher than the former. Based on the final logistic regression model we plotted the variables operative procedure, prophylactic

TABLE 6. *Odds Ratios for Operative Mortality for 763 Patients Operated On for Stomach Cancer*

Variable	Odds Ratio	p Value	95% CI
Sex		0.005	
Women	1		
Men	2.33		1.26–4.31
Age		0.0001	
x	1		
x + 10	2.24		1.61–3.13

antibiotics, sex, and splenectomy against age, and the results are given in Figures 1–4.

The logistic regression analysis was repeated with operative mortality as the dependent variable. The final model (which fitted the data well; $p = 0.43$) revealed that sex ($p < 0.001$) and age ($p < 0.001$) were the only variables that independently influenced postoperative death. The results are visualized in Figure 5. Men had a higher postoperative mortality rate than women. Postoperative mortality increased almost exponentially with age.

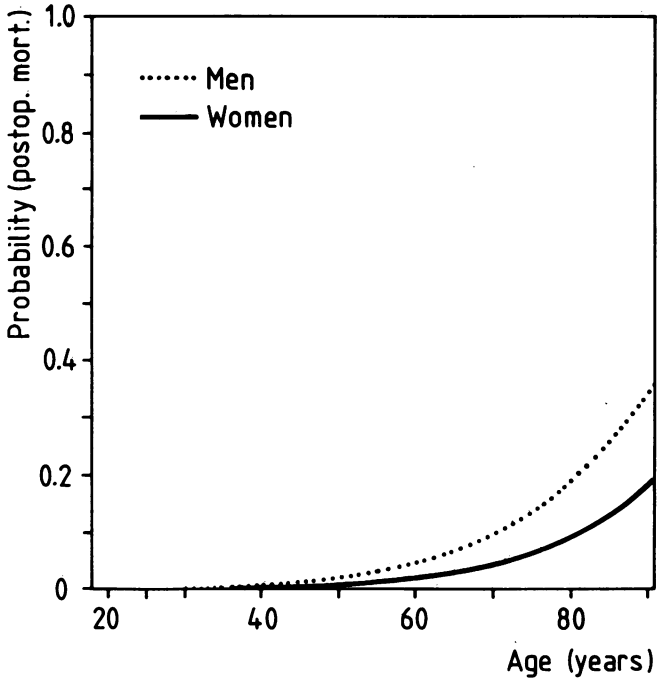

FIG. 5. Probability of operative mortality for men and women according to age.

Discussion

Several strategies should be explored to improve survival after surgery for gastric cancer. A reduction in operative mortality for patients undergoing a potential curative resection would clearly be beneficial, and interest should be focused on studies aimed at identification of pre- and intraoperative variables which are linked to postoperative complications and mortality. Factors assumed to predispose to complications include technical skill of the surgeon, operating time, malnutrition and age, prophylactic antibiotics as well as operative procedure performed.[17,18]

Most studies on complications after gastric surgery analyze possible predictive factors in a univariate manner, not taking the multivariate nature of this problem into account.[17–20] The limitations of such analyses are illustrated by the two-way cross-tabulations summarized in Table 4, which revealed six factors associated with complications and two related to postoperative mortality. However, the multivariate analyses reduced the number of true significant associations. More importantly, the multivariate analyses also identified variables clearly associated to complications that were not demonstrated by simple cross-tabulation and chi-square statistical analyses, as demonstrated for the variable prophylactic antibiotics (Tables 4 and 5). The reason for this discrepancy might be explained by interactions between the variables. Such findings also suggest that conclusions drawn on the basis of simple cross-tabulations and statistical analyses should be interpreted with care.

Previous studies have shown increasing complication and mortality rates with age,[21,22] whereas others have challenged this finding.[18] In the current study, age was a major determinator with respect to postoperative complication and mortality (Figs. 1–5). Further, men had higher risks than women for all types of complications such as anastomotic leak and bleeding, as well as general complications. A higher postoperative mortality rate for men than for women has also been demonstrated by Miwa,[23] but so far, no hypothesis has been proposed that can explain this finding. Detailed analyses of our data have not uncovered any mechanism that might explain the clear excess risk for men undergoing gastric surgery for cancer.

As reported by others[1,24] we found that the type of operation affected the complication rate, *i.e.*, was higher for extensive procedures (like total gastrectomy) than for distal resection. This is an important conclusion as a potential increase in postoperative long-term survival is expected to follow more extensive operations. However, the survival advantage of an extensive operation performed *de principe* is still a matter of discussion.[25,26]

Some surgeons suggest that a minor surgical procedure as proximal resection for upper-third tumors is the treatment of choice. However, for the last two decades it has been known that proximal resection carries a higher complication rate than total gastrectomy.[1,3,10,24] This finding was confirmed in the current study, which demonstrated alarmingly high complication risks (Fig. 2) for this procedure. It was noted that septic and general complications were especially common after proximal resection. We do not find proximal resection to be any easier to perform than a total gastrectomy, and we recommend the latter procedure for all proximal tumors.

Removal of the spleen *en bloc* with the gastric specimen has traditionally been part of a standard radical gastric resection for cancer. Recently it has been sug-

gested that splenectomy might have a detrimental effect on survival.[27] However, other studies have not been able to confirm the negative effect of splenectomy.[28] In this study we found an increased rate of complication after splenectomy. Whether splenectomy was performed or not did not have any influence on operative mortality.

Administration of prophylactic antibiotics reduced postoperative complications by approximately 10% (Table 3 and Fig. 4). A full discussion about the value of antibiotic prophylaxis in gastrointestinal tract surgery is beyond the scope of this paper. However, based on our data we conclude that any gastric resection for cancer should be covered by prophylactic antibiotics.

Malnutrition has for a long time been recognized to be associated with increased complication and operative mortality rates.[22,29] In this study, weight loss did not have an influence on complications and mortality. The explanation behind this rather controversial conclusion is probably that malnourished patients most often have advanced disease not suitable for resection.

Resection for stomach cancer often implies major surgery for patients at an increased risk. For this reason it might be expected that the level of care would influence patient outcome. We were, however, not able to discover any association between hospital level, complication, and operative mortality. The figures were, however, of borderline significance, with a lower complication rate for county hospitals than for university and local hospitals.

The overall operative mortality rate of 8.3% for resected patients found in this study is in accordance with that of most reported studies from the Western world.[1,2,4,7] Further, it should be noted that the mortality rate after total gastrectomy was comparable to the mortality rate after distal resection (7.7% *vs.* 6.9%). Japanese results are, however, far better,[8,9] and we should aim at reduced operative mortality rates as this will have a substantial impact on long-time survival. The only factors found to predict mortality were sex and age, whereas operative procedure and hospital group were at the borderline of significance.

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Appendix

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* Member of the working party.