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Morbidity Prediction Using Pre- and Intraoperative Data

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Preoperative and intraoperative information about patient status was collected for 66 general surgical patients receiving general anesthesia who had independent objective measurements of postoperative morbidity. Data included information collected during preoperative patient visits, such as age, blood pressure, and ASA physical status scores. Intraoperative information was of two types: 1) manually recorded descriptors of the operative course, such as blood loss and duration of operation, and 2) heart rate and blood pressure recorded every one or two minutes by an automatic patient-monitoring system. The postoperative outcome was assessed by each patient's senior nurse, who assigned a weighted morbidity score to each of six organ systems during a structured interview on the seventh postoperative day.

No hospital death occurred in the series. A third of the patients were scored as having experienced some postoperative morbidity. Six of the 64 manually collected preoperative descriptors were significantly associated with positive morbidity scores. These variables related to preoperative hypertension and duration of operation. Fifty of a series of 190 statistical descriptors of the anesthetic course were associated with morbid outcomes. Statistics that described the variability of intraoperative cardiovascular status were most often found to have significant associations with postoperative morbidity.

Using all information available at the end of anesthesia, a discriminant function that correctly predicted outcome for 83 per cent of the patients was developed. Variability of intraoperative physiologic status was shown to be an important predictor of morbid outcome. Eventually, outcome predictions such as these may be used to assign different postoperative therapeutic regimens to different patients, depending on need and expected outcome. (Key words: Anesthesia: morbidity; hazards; outcome prediction. Complications.)

A PREDICTION of postoperative outcome is made when the patient is counseled for an operation and anesthetic management is planned. Such a prediction is based on preoperative assessment and the proposed surgical and anesthetic interventions, but it relies more on personal experience than on statistical analyses. Accordingly, outcome studies that measure more than mortality are needed even though their design is beset by the difficulties inherent in defining morbidity.

In the Institutional Differences Study,[1] postoperative patient outcomes were reported for both morbidity and mortality. Morbidity measurement was based upon the assignment of a rating score to each of six or more major patient organ systems by the patient's senior nurse on the seventh post-operative day. This morbidity score was a variation of the Nursing Assignment Index described by Owens *et al.*[2] Usual predictors of postoperative morbidity and mortality include the age and ASA physical status,[3] factors that describe the patient's physiologic condition. We postulate that patients' cardiovascular responses to anesthesia and operation may be another important expression of physiologic status. To examine this possibility, we collected preoperative and intraoperative physiologic information for a series of patients, and from it developed a function predictive of postoperative outcome.

Methods

Adult general surgical patients who received general anesthesia for surgical procedures that lasted 30 min or longer were studied. Four rooms in our surgical suite are devoted to adult general surgery. Two of them were instrumented for this study. One of these rooms was used primarily by attending surgeons and the other by the house staff. First-case priority within these two sets of surgeons varied from day to day. Scheduling was done with no regard to this study. In general, the first patient scheduled in the morning for either or both of these rooms was studied.

The study group consisted of 36 female patients (average age 51 years, range 14–83) and 30 male patients (average age 53 years, range 18–80). During the course of the study we were unable to obtain complete physiologic data for six patients because of transducer or calibration difficulties, and an accident resulted in erasing from disk storage a block of data for eight patients. Complete information was collected for 66 otherwise consecutive patients, and forms the basis for this study. Preoperative patient condition was assessed by completing a data sheet at the time of preoperative rounds. We recorded the age, sex, weight, blood pressure, temperature, operation and ASA physical status score for each patient (table 1). The patient's primary occupation and amount

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of schooling were recorded, as well as whether he lived alone. We also recorded whether the patient had received anesthesia previously and an estimate of the severity of preoperative complications existing in 12 organ systems. The anesthesiologist was asked to use his best judgment to score disability in each organ system, *i.e.*, none, mild, moderate, or severe preoperative disease. The specific diagnoses and conditions that led to the classification by the anesthesiologist were not recorded. Similarly, the preoperative electrocardiogram and chest roentgenogram were classified as normal, abnormal but of no particular concern, or abnormal and of concern to the anesthesiologist. In addition, we asked both the anesthesiologist who administered the anesthetic and the operating surgeon to estimate, on a scale of 1 to 4, the severity of the patient's illness and the probable postoperative outcome. The authors participated in the administration of anesthesia and the patient status assignments. In all, 34 preoperative risk factors were recorded for each patient.

One portion of the intraoperative data was collected from the anesthesia record. This included the type of anesthesia, an estimate of the adequacy of premedication, and whether an opiate, muscle relaxant, anticholinergic agent, or endotracheal tube was employed. We recorded the time of anesthesia, defined as the time from the beginning of the preparation of the patient in the operating room to the delegation of responsibility for his monitoring to the recovery room staff, and the duration of operation from incision to the application of the dressing. The intraoperative blood loss and urinary output were recorded, along with diagnoses, procedures, and identifying code numbers for both the surgeon and the anesthesiologist. At the end of the procedure the anesthesiologist was asked to record his subjective estimate of both the severity of intraoperative complications and the patient's condition when leaving the operating room. In all, 30 intraoperative descriptors were recorded.

Intraoperative blood pressure and pulse data were automatically collected by a computer-centered patient-surveillance system.[4] This noninvasive system collected systolic and diastolic blood pressure every two minutes and pulse rate, temperature, inspired oxygen tension, and ear blood oxygen saturation each minute. Blood pressure was measured with a Roche 1216 Arteriosonde and pulse rate was derived by computer algorithm from the electrocardiogram. Monitoring data were displayed in the operating room and also cabled to an adjacent PDP 11/20 computer system. Computer programs were used to generate time-base

TABLE 1. The Study Population*

Operation	ASA Physical Status Score			
	I	II	III	IV
Cholecystectomy	5	6	4	
Inguinal herniorrhaphy	5	2		
Breast biopsy	4	2	1	
Laparotomy	3	3	1	
Major vascular		4	2	
Colostomy		3	2	
Colectomy	1	2		
Mastectomy	1		1	
Splenectomy	1	1		
Skin graft		2		
Vein stripping		2		
Sympathectomy		1		
Pancreaticoduodenectomy		1		
Parotidectomy	1			
Thyroidectomy	1	1		
Gastrectomy		1		
Amputation (below knee)				1
Parathyroidectomy		1		
	22	32	11	1

* Operations performed and ASA physical status scores for patients in the experimental group. All were elective operations; no patient was assigned an ASA physical status score of V.

trend graphs for display in the operating room and to store the data for later statistical analyses. Generally, two baseline blood pressure and heart rate measurements were collected before the injection of drugs or the induction of anesthesia. Monitoring was continued until the patient was transferred to the recovery room. Occasionally, an obviously incorrect blood pressure measurement was obtained by the Arteriosonde and not rejected by the logic circuitry of the instrument. This most often happened early in the operation, during positioning and preparation of the patient. These outliers were identified and manually removed from the data files before statistical analysis.

From the three physiologic variables directly measured during anesthesia, heart rate and systolic and diastolic blood pressure, two derived variables were calculated, the pulse pressure and a cardiac work index (systolic blood pressure times heart rate). Each of the five intraoperative variables was then summarized over the period of anesthesia by a variety of statistical measures (Appendix 1). Additionally, each statistical measure was calculated twice for each patient, once using all data available during anesthesia and a second time using only data from the maintenance period. The maintenance period was defined as beginning 8 minutes after injection of succinylcholine when endotracheal tubes were used and 8 minutes after injection of an induction dose of thiopental for other cases. The statistical summary of pulse

TABLE 2. Population Differences in Manually Collected Data*

	Morbid Mean ± SD	Not Morbid Mean ± SD
Preoperative heart rate (beats/min)	77 ± 12	84 ± 9
Preoperative systolic blood pressure (torr)	150 ± 27	132 ± 20
Anesthesia time (min)	194 ± 64	153 ± 76
Operation time (min)	166 ± 62	121 ± 68
Anesthetics within previous year	32 per cent yes	9 per cent yes
Sex	68 per cent male	32 per cent male

Significance of all variables is at the .05 level.

* Six of the 64 patient descriptors obtained from the patient interview, the surgeon, the patient's chart and the anesthesia record were found to have significant associations with morbid patient outcome.

and blood pressure data included 190 elements per case.

An independent assessment of postoperative morbidity was made either on the seventh postoperative day or as soon after discharge as possible when the patient was discharged prior to the seventh postoperative day. This assessment was made by a specially trained nurse–observer, who obtained information by interviewing the senior clinical nurse who had cared for the patient during his hospital stay. This Nursing Assessment Index was based upon an assignment of a weighted score, from 0 for no impairment to 3 for major disease, to each of six or more major organ systems (cardiovascular, respiratory, central nervous, kidney or urinary, liver or biliary, gastrointestinal and other). This measurement was adapted from a report from Owens *et al.*,[2] where it was shown to have a highly significant correlation with postoperative mortality. All presently reported morbidity is in terms of the Nursing Assessment Index.

Since our initial study group necessarily included only a limited number of patients, we were constrained to morbidity measures that could be expected to identify a substantial minority of patients as morbid. Additionally, we agreed to consider only adaptations of previously investigated measures of morbidity. Consequently, we classified patients as morbid when they manifested one or more systemic complications apparent to the division nurse on or before the seventh postoperative day. When a patient was discharged before the seventh day, a morbidity score was obtained by interviewing the appropriate nurse on the day following discharge. Our morbidity outcome score thus represents an adaptation of the Nursing Assessment Index described, wherein patients discharged prior to the seventh postoperative day were deleted from the study population.

Including the preoperative variables, the intraoperative code sheet variables, and the statistical summaries from the intraoperative physiologic variables, each patient provided 254 potential risk factors for postoperative morbidity. As the first step, each of these potential risk factors was examined to determine univariate relationships with seventh-postoperative-day morbidity measurements. Thirteen of these variables (5 per cent) should have shown significant relationships at the .05 level on the basis of chance. We found 56 significant variables and proceeded with further analysis.

A multivariate statistical analysis was performed to determine a minimal set of the 254 potential risk factors sufficient for predicting postoperative morbidity. Due to the large number of variables available, several preliminary analyses on various subsets of the variables were necessary. These preliminary analyses identified many variables as not being important for prediction and also produced a subset of the potential risk factors that could be simultaneously analyzed by stepwise discriminant analysis. Discriminant analysis estimates weights for risk factors in order to produce an equation predictive of the morbid and non-morbid outcome. This stepwise analysis resulted in a further decrease in the number of potential risk factors, allowing the computation of all possible discriminant functions[6] for 16 potential risk factors. The all-possible-discriminant function analysis resulted in a final subset of six risk factors. Ultimately, the predictive ability inherent in the final six risk factors was estimated by the "leaving-one-out" method described by Lachenbruch.[7]

Results

Twenty-two of the 66 patients in the experimental group had outcome scores of 1 or more and thus constituted the morbid group. Forty-four patients had scores of zero and were therefore considered not morbid. No hospital death occurred. Significant univariate association was found between six of the 64 manually recorded patient risk classifiers and postoperative morbidity (table 2). Fifty of the 190 statistics calculated from the automatically recorded intraoperative pulse and blood pressure measurements were shown to have significant ($P < 0.05$) univariate association with outcome (Appendix II). In general, the significant ($P < 0.05$) manually recorded variables related to preoperative hypertension and to the length of operation, while the intraoperative variables related to the variability of heart rate and blood pressure during anesthesia.

The six most important risk factors that emerged from the discriminant analyses are presented in table 3. In clinical terms, these results show that patients in this series tended to have measurable postoperative morbidity when they had increased systolic blood pressure values preoperatively and had received general anesthesia in the previous year. When the absolute value of a measure of skewness of systolic blood pressure and pulse pressure was high, the probability of morbidity also increased. When the *absolute* value of skewness is high the patient experiences more high *or* low pressure values than would be expected from a normal distribution. These extreme values will generally be in the same direction in the same patient, but may be in different directions in different patients. Finally, when the cumulative sum of the differences (CUSUM)[8,9] between the individual systolic blood pressures or cardiac work measures and their intraoperative averages were large negative numbers, the probability of morbid outcome was even higher. These cumulative-sum statistics describe a decrease in the values for systolic blood pressure and our measures of cardiac work as anesthesia progressed.

The quality of the morbidity prediction based upon the six risk factors was assessed by estimating the probabilities of correctly classifying a patient who will in fact experience morbidity and a patient who will not. An overall average 83 per cent correct classification was found in either category (table 4). Given these six risk factors, the inclusion of additional variables into the predictive function did not significantly improve the accuracy of the outcome prediction.

Discussion

Because of the difficulties involved in defining morbidity, we wanted to compare the incidence of morbid outcomes found in our study with the incidences found in other larger studies. Re-examination of the data presented by Owens *et al.* shows that of their 1,053 patients still hopitalized on the seventh postoperative day, 503, or 49 per cent, had Nursing Assessment Indices of 1 or more and would thus have been classified as morbid by our rule. When their patients discharged before the seventh postoperative day are classified as not morbid, 503 of 3,217, or 16 per cent of the postoperative patients, had measurable morbidity. The Institutional Differences Study reported an overall 20.2 per cent combined incidence of moderate to severe morbidity on the seventh postoperative day or postoperative death within 40 days. These data came from the intensive study of about 8,500 selected general surgical patients. Data from our smaller patient population show a 33 per cent incidence (22 of 66 patients) of measurable postoperative morbidity. Operative procedures less than 30 minutes in duration were judged to produce too little intraoperative information and were not studied. Thus, our incidence of detectable morbidity, regardless of discharge date, in a series of general surgical patients who had lengthier operations is somewhat larger than those in prior published results. The reasons for the differences are not apparent, but they may have been due in large part to the fact that the patient populations were not similar.

The analysis of manually collected preoperative information produced no unexpected result (table 2). Most anesthesiologists would expect a high incidence or postoperative morbidity in hypertensive patients subjected to long operations. The higher incidence of morbid scores in male patients is not reported elsewhere and needs further clarification.

It is our clinical impression that intraoperative vital signs tend to be more stable in young, healthy patients than in elderly or otherwise more fragile patients with lesser physiologic reserves. Patients who have nonvarying vital signs during anesthesia are usually expected to have less postoperative morbidity than patients with markedly unstable intraoperative values. This clinical impression is strongly supported by the univariate analysis of automatically obtained intraoperative data (Appendix II). Generally, statis-

TABLE 3. Classification Variables*

1) Systolic blood pressure, maintenance, negative CUSUM
2) Pulse pressure, maintenance, absolute value of skewness
3) Systolic blood pressure, all, absolute value of skewness
4) Cardiac work index, all, negative CUSUM
5) Preoperative systolic blood pressure
6) Anesthesia within previous year

The six risk factors that resulted from the analyses of the total set of 254 risk factors available at the end of anesthesia. These variables define the predictive function that produced the classification matrix in table 4. The CUSUM and skewness values that describe the maintenance of anesthesia, as well as those describing the entire course, are found to be predictive, as are two preoperative patient status descriptors.

TABLE 4. Classification Matrix*

	Predicted Not Morbid	Predicted Morbid	Total	Per Cent Correct
Not morbid outcome	37	(7)	44	84
Morbid outcome	(4)	18	22	82
TOTAL	41	25	66	83

A classification matrix in which predicted outcome is compared with actual patient outcome. An overall 83 per cent correct prediction results when the six risk factors listed in table 3 are used in a discriminant function constrained to equalize the number of morbid and not-morbid misclassifications.

tical measures of short-term dispersion of data, such as standard deviation and skewness, and measures of long-term dispersion, such as CUSUM, have the most significant associations with postoperative outcomes.

Heart rate alone, while sampled at twice the frequency of blood pressure, did not provide any statistical summary for the subset of six most important risk factors. Similarly, diastolic blood pressure alone was not important. Statistical summaries from both the maintenance period and the entire course of anesthesia are clearly necessary for optimal discrimination. This, in turn, suggests that the patterns of physiologic responses are indeed different in the induction and maintenance phases of anesthesia.

The leaving-one-out method of estimating the probabilities of misclassification as presently used is less optimistically biased than the simple resubstitution method[10] and is thus a good way to test our conclusions using our present patient sample. The estimates presented may still be optimistic due to the large number of potential risk factors examined. On the other hand, refined measures of intraoperative instability, especially those taking into account the physiologic differences between the induction and postinduction periods of anesthesia, may result in increased probabilities of correct classification. A linear discriminant function is of value to the physician wishing to anticipate the postoperative morbidity or non-morbidity of his patients (table 4).

A powerful statistical tool, discriminant analysis, was used in this study to identify risk factors associated with poor outcome. The cumulative sum was found to be an important statistic descriptive of the intraoperative course. Calculation of these unfamiliar numbers represents no threat to the future clinician, since multivariate analyses are not needed once risk factors are determined and miniature computers can now easily manage CUSUM, skew and other descriptive statistics essentially as quickly as the data can be gathered. This analysis has shown that statistical descriptions of the variability of the patient's physiologic state are important in calculating the probability of poor outcome. Adding these new descriptions to present predictors such as age and ASA physical status score should allow earlier, more accurate prediction of outcome.

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APPENDIX I. Statistical Summaries Calculated for Each Set of Automatically Collected Intraoperative Data

Measures of location
1. Mean
2. Median

Measures of dispersion
1. Standard deviation
2. Median deviation
3. Semi-intraquartile range
4. Largest change
5. Absolute value of largest change
6. Skewness
7. Absolute value of skewness
8. Kurtosis

Measures of autocorrelation
1. First-order autocorrelation
2. Second-order autocorrelation
3. Third-order autocorrelation
4. Number of turning points

Measures of location shift
1. Maximum positive CUSUM*
2. Minimum negative CUSUM
3. Maximum two-sided CUSUM

Measures of trend
1. Spearman's rho
2. Absolute value of Spearman's rho

* The target value for the CUSUM was taken to be the intraoperative mean.[11]

APPENDIX II. Univariately Significant Summary Statistics, Those Statistics That Associate the Automatically Collected Intraoperative Data with a Morbid Postoperative Course

	Morbid Mean ± SD	Not Morbid Mean ± SD
A. Systolic blood pressure		
1. Maintenance data		
a. Standard deviation	15.0 ± 7.1	11.8 ± 4.7
b. Median deviation	10.7 ± 6.1	6.9 ± 3.2
c. Semi-intraquartile range	11.2 ± 6.4	7.6 ± 3.7
d. First-order serial correlation	5.83 ± 2.09	4.50 ± 2.20
e. Second-order serial correlation	4.59 ± 2.24	3.44 ± 1.95
f. Third-order serial correlation	3.87 ± 1.93	2.65 ± 1.78
g. Positive CUSUM	75.5 ± 58.3	43.3 ± 27.5
h. Negative CUSUM	79.3 ± 56.3	43.8 ± 26.6
2. All data		
a. Median deviation	11.1 ± 5.9	7.7 ± 2.6
b. First-order serial correlation	6.37 ± 1.47	5.03 ± 1.78
c. Second-order serial correlation	5.04 ± 1.90	3.87 ± 1.75
d. Third-order serial correlation	4.09 ± 1.85	2.99 ± 1.80
e. Positive CUSUM	89.3 ± 58.1	52.4 ± 31.2
f. Negative CUSUM	92.9 ± 54.4	57.2 ± 31.2
B. Diastolic blood pressure		
1. Maintenance data		
a. First-order serial correlation	5.39 ± 1.64	4.28 ± 2.28
b. Third-order serial correlation	3.50 ± 1.65	2.34 ± 1.92
c. Positive CUSUM	48.5 ± 32.5	31.8 ± 20.1
d. Negative CUSUM	48.6 ± 26.8	31.8 ± 18.7
e. Absolute value of Spearman's rho, standardized	4.31 ± 3.27	2.51 ± 2.22
2. All data		
a. Third-order serial correlation	3.61 ± 1.70	2.40 ± 2.06
b. Positive CUSUM	53.4 ± 33.6	36.6 ± 22.7
c. Negative CUSUM	50.6 ± 24.5	37.3 ± 21.5
d. Absolute value of Spearman's rho, standardized	4.11 ± 3.06	2.66 ± 2.22
C. Heart rate		
1. Maintenance data		
a. First-order serial correlation	11.2 ± 2.8	9.3 ± 3.3
b. Two-sided CUSUM	54.5 ± 49.5	19.1 ± 64.5
c. Spearman's rho, standardized	−11.6 ± 13.3	−5.2 ± 10.1
2. All data		
a. First-order serial correlation	11.9 ± 2.7	10.1 ± 3.2
b. Two-sided CUSUM	54.0 ± 64.2	10.6 ± 80.5
c. Spearman's rho, standardized	−8.68 ± 9.47	−3.59 ± 9.29
D. Pulse pressure		
1. Maintenance data		
a. Mean	43.8 ± 16.2	35.6 ± 13.3
b. Median	43.6 ± 16.8	35.0 ± 12.9
c. Standard deviation	10.4 ± 5.0	8.1 ± 2.8
d. Median deviation	7.00 ± 3.64	4.82 ± 1.83
e. Semi-intraquartile range	7.34 ± 3.64	5.14 ± 1.98
f. Kurtosis	−0.21 ± 0.87	0.55 ± 1.53
g. First-order serial correlation	4.21 ± 2.02	3.09 ± 1.93
h. Second-order correlation	3.45 ± 2.16	2.22 ± 1.92
i. Third-order serial correlation	2.67 ± 2.05	1.69 ± 1.75
j. Positive CUSUM	45.2 ± 31.0	25.4 ± 14.6
k. Negative CUSUM	48.7 ± 33.3	25.4 ± 14.4

	Morbid Mean ± SD	Not Morbid Mean ± SD
2. All data		
a. Mean	44.9 ± 16.3	37.1 ± 13.0
b. Median	44.2 ± 17.1	35.6 ± 12.9
c. Median deviation	7.32 ± 3.43	5.36 ± 1.76
d. Semi-intraquartile range	7.55 ± 3.49	5.92 ± 1.97
e. First-order serial correlation	4.92 ± 1.69	3.61 ± 1.78
f. Second-order serial correlation	4.09 ± 1.91	2.68 ± 1.82
g. Positive CUSUM	53.9 ± 33.0	33.3 ± 18.1
h. Negative CUSUM	61.3 ± 37.2	35.5 ± 19.1
E. Cardiac work index		
1. Maintenance data		
a. First-order serial correlation	5.96 ± 1.79	4.77 ± 2.24
2. All data		
a. First-order serial correlation	6.19 ± 1.50	5.20 ± 1.89

Significance of all variables is at the .05 level.