PAPER

Temporal Patterns of Postoperative Complications

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Hypothesis: A variety of major complications occur after intra-abdominal operations. Knowledge of when specific complications occur during the postoperative period would be useful in their diagnosis, prevention, and management. Our aim was to determine the incidence of major complications during specific postoperative intervals.

Design: One thousand twenty-one patients undergoing intra-abdominal operations were studied postoperatively as part of a randomized clinical trial. Thirteen defined major complications were sought at the following specific intervals: less than 1, 1 through 3, 4 through 7, and 8 through 30 days after the operation.

Setting: Cooperative trial from 15 Veterans Affairs medical centers.

Interventions: Intra-abdominal aortic, gastric, biliary, and colonic procedures.

Main Outcome Measurements: Major postoperative complications.

Results: Four hundred thirty-five major complications were diagnosed within 30 days of the patients' being operated on. Seventy-four (17%) occurred within 1 day, 185 (43%) between 1 and 3 days, 72 (17%) between 4 and 7 days, and 104 (24%) between 8 and 30 days. Three deaths (8%) occurred within 1 day, 3 (8%) in 1 through 3 days, 4 (11%) in 4 through 7 days, and 27 (73%) in 8 through 30 days. The greatest risk of hypotension (43%), myocardial infarction (47%), and respiratory depression (55%) was within 1 day. The highest incidence of congestive heart failure (46%), pulmonary embolus (50%), and respiratory failure (76%) occurred at 1 through 3 days. Pneumonia (38%) was most common at 4 through 7 days. Cerebrovascular accident (53%) and sepsis (71%) occurred preponderantly at 8 through 30 days. Renal failure had a bimodal distribution with maxima at 1 through 3 days (31%) and 8 through 30 days (56%). The risk of cardiac arrhythmia and gastrointestinal tract bleeding was similar throughout all intervals.

Conclusions: While major complications occur throughout the postoperative period, the highest incidence is 1 through 3 days after the operation. However, specific complications occur in the following distinct temporal patterns: early postoperative, several days after the operation, throughout the postoperative period, and in the late postoperative period. Knowledge of these patterns should aid clinical management.

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A VARIETY of major complications occur after intra-abdominal operations.[1-4] These events prolong the patient's length of stay in the hospital, consume greater health care resources, and may lead to the patient's death. The risk of postoperative complications is influenced by preoperative factors, intraoperative events, and postoperative aspects of care. Thus, strategies for improving surgical outcome include optimizing the preoperative status of the patient, avoiding adverse intraoperative events, and instituting interventions to prevent postoperative complications. Detecting adverse events early in their course and treating them with effective therapies will also improve patient outcome.

Knowledge of when specific complications occur throughout the postoperative period would be useful in their diagnosis, prevention, and management. More intense surveillance might be carried out at specific times to promote earlier detection. Preventive strategies could become more focused. Finally, the temporal occurrence of a complication might have causative and therapeutic implications. The aim of this study was to determine the incidence of major complications during specific postoperative intervals.

METHODS

PATIENTS

One thousand twenty-one patients undergoing intra-abdominal operations were studied prospectively during the postoperative period as part of a randomized clinical trial of 15 Veterans Affairs medical centers.[5] Patients included men older than 21 years who were categorized as American Society of Anesthesiologists (ASA)

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classification III (ie, a patient with severe systemic disease–limiting but not incapacitating activity) or IV (ie, a patient with incapacitating systemic disease) preoperatively and who required hospitalization postoperatively.[6] Patients were excluded from the study if they required emergent procedures, had a documented myocardial infarction (MI) in the past 6 months, had an abdominal procedure within the past 3 months, were receiving chemotherapy or immunosuppressive therapy, had a tracheostomy, or endotracheal intubation.

This was a cooperative trial from 15 Veterans Affairs medical centers. The study protocol was approved by the Veterans Affairs Cooperative Studies Program and local institutional review boards in the participating medical centers. Patients gave informed consent before their enrollment in the study. The members of the study group who participated in the study have been described elsewhere.[5]

MAJOR COMPLICATIONS

The following 13 defined major complications were sought at specific intervals: less than 1, 1 through 3, 4 through 7, and 8 through 30 days after the operation. These 13 major complications were defined as follows.

1. New MI: An increase in the serum concentration of the myocardial-specific isoenzyme fractions of creatine kinase MB fraction (CK-MB) and lactic dehydrogenase as evidenced by a CK-MB/creatine kinase ratio being 5% or more and/or the following electrocardiographic changes: a typical new persistent elevation/depression of the ST segment and/or a new Q wave of greater than 0.04 seconds in duration with its depth more than 25% of the amplitude of the succeeding R wave in limb leads, or any new Q wave in V_1 through V_3.

2. Newly Developed or Significantly Worsened Congestive Heart Failure: Dyspnea, basilar rales on lung auscultation and/or an S_3 gallop, and confirmation by radiographic changes of pulmonary congestion and/or a pulmonary capillary wedge pressure greater than 20 mm Hg, that requires pharmacologic therapy (ie, digitalis, diuretic agents, and others).

3. Severe Hypotension (Including Cardiac Arrest): Mean arterial pressure less than 50 mm Hg, signs of cerebral hypoperfusion or a cardiac index of less than 2.0 L/min per square meter for longer than 10 minutes that requires pharmacologic treatment and/or resuscitation.

4. Arrhythmia: Ventricular tachycardia that lasts longer than 30 seconds and requires pharmacologic therapy. Atrioventricular block that requires placement of a pace maker.

5. New Angina Pectoris: A typical chest pain that physicians caring for the patient felt to represent new angina, requiring pharmacologic therapy.

6. Respiratory Failure: The need for intubation and mechanical ventilatory assistance for more than 24 hours postoperatively or the need for reintubation and mechanical ventilatory assistance after 1 hour postoperatively.

7. Pneumonia: The presence of a new infiltrate seen on the chest radiograph, plus 2 of the following 3 clinical findings: a temperature higher than 38°C, an abnormal elevation of the white blood cell count, or a pathogen identified in the sputum by gram stain and culture that requires intravenous antibiotic treatment.

8. Respiratory Depression (Including Arrest): A new postoperative respiratory depression with a PaCO, of greater than 60 mm Hg that physicians caring for the patient felt was associated with an administration of postoperative narcotic, requiring pharmacologic (naloxone hydrochloride) treatment or intubation.

9. Pulmonary Embolism: An acute onset of dyspnea and tachypnea, hypotension, and increased central venous pressure, positive ventilation-perfusion scan and/or pulmonary angiogram (if performed), requiring medical treatment.

10. Sepsis: The presence of a localized infection together with a postive blood culture for the same pathogen plus clinical evidence of bacteremia with chills, rigors, fever, and an elevated white blood cell count, requiring intravenous antibiotic treatment.

11. Renal Failure: A serum creatinine level greater than 3.0 mg/dL (265 µmol/L) and doubling of baseline value, or the need for dialysis.

12. New Cerebral Hypoxia, Thrombosis, or Intracranial Hemorrhage: The occurrence of new neurologic dysfunction (hemiplegia, hemianesthesia, hemianopia, aphasia, or unconsciousness).

13. Gastrointestinal Bleeding: The sudden appearance of frank blood either on nasogastric lavage or by rectum, with a subsequent decrease in the hemoglobin level of 2 g/dL or greater, with no other known or suspected source on ongoing blood loss.

PROCEDURES

Operations included open intra-abdominal aortic, gastric, biliary, and colonic procedures. All patients received general anesthesia with isoflurane and/or fentanyl citrate with endotracheal intubation. Vecuronium bromide was used for muscle relaxation as necessary. Postoperative pain management was via intermittent parenteral narcotics, epidural morphine, or both. By design half of the patients received supplemental epidural anesthesia and analgesia. Other aspects of anesthetic care were as described previously.[5]

All patients received prophylactic antibiotics before the operation and for 24 hours postoperatively. Patients undergoing colon procedures had their bowel cleansed mechanically and received either oral or parenteral antibiotics. Other aspects of surgical care were at the discretion of the surgeon.

Patients had a 12-lead electrocardiogram done routinely on the first and third postoperative days. Total serum creatine phosphokinase levels and MB isoenzymes were measured every 12 hours for 3 days after the operation. Other diagnostic tests and procedures were obtained as determined by the clinicians involved.

We used the contingency table method to test for significant differences in the proportion of patients in the different groups. Statistical significance was set at $P<.05$, 2-tailed.

RESULTS

The study included 1021 men with an mean (SD) age of 67 (9) years. Operations performed included colonic (n=399), aortic (n=374), biliary (n=98), gastric (n=77), and other intra-abdominal (n=36) procedures. Thirty-seven patients did not undergo an operation. Nine hundred thirty-one patients were classified as being ASA III and 89 as ASA IV. Goldman risk index was 0 to 5 in 496 patients, 6 to 12 in 446 patients, and 13 to 26 in 79 patients. Preoperative medical characteristics are given in **Table 1**. Patients undergoing aortic procedures were similar to those having nonaortic procedures for age (mean [SD] age, 67 [8] vs 67 [9] years) and ASA classification (90% vs 92% ASA III). Patients with aortic conditions were more likely to be hypertensive, have chronic obstructive pulmonary disease, and be smokers but were less likely to have diabetes mellitus but to have a history of alcoholism than patients without aortic conditions (Table 1).

Four hundred thirty-five major complications were diagnosed within 30 days of operation (**Table 2**. Two hundred two (20%) of 1021 patients experienced 1 or

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Table 1. Preoperative Characteristics*

Characteristic	Aortic Procedures (n = 374)	Nonaortic Procedures (n = 647)	Total No. of Procedures (N = 1021)
Hypertension	241 (64)	328 (51)†	**569** (56)
Smoker (currently)	183 (49)	209 (32)†	**392** (38)
COPD	137 (37)	193 (30)†	**330** (32)
Previous myocardial infarction	109 (29)	164 (25)	**273** (27)
Diabetes mellitus	69 (18)	159 (25)†	**228** (22)
Alcoholism (history)	58 (16)	142 (22)†	**200** (20)
Arrhythmia	68 (18)	126 (19)	**194** (19)
Stroke	64 (17)	84 (13)	**148** (15)
Angina pectoris	62 (17)	82 (13)	**144** (14)
Previous congestive heart failure	39 (10)	62 (10)	**101** (10)
Asthma	4 (1)	26 (4)	**30** (3)
Alcoholic-induced liver disease	2 (1)	23 (4)	**25** (2)
Renal failure	3 (1)	9 (1)	**12** (1)

Abbreviations: ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease.

*Data are given as the number (percentage) of patients. Some patients had more than 1 characteristic.

†$P<.05$ vs aortic procedures.

Table 2. Incidence of Complications*

Variable	Aortic Procedures (n = 374)	Nonaortic Procedures (n = 647)	Total No. of Procedures (N = 1021)
Cardiac			
Myocardial infarction	20 (5)	25 (4)	**45** (4)
Congestive heart failure	23 (6)	12 (2)†	**35** (3)
Hypotension	17 (5)	13 (2)†	**30** (3)
Cardiac arrhythmia	11 (3)	10 (2)	**21** (2)
Angina	4 (1)	1	**5** (1)
Pulmonary			
Respiratory failure	79 (23)	44 (7)†	**123** (12)
Pneumonia	27 (7)	41 (6)	**68** (7)
Respiratory depression	8 (2)	12 (2)	**20** (2)
Pulmonary embolus	2 (1)	0	**2**
Other			
Sepsis	16 (4)	22 (3)	**38** (4)
Renal failure	9 (2)	7 (1)	**16** (2)
Cardiovascular accident	10 (3)	7 (1)	**17** (2)
Gastrointestinal tract bleeding	7 (2)	8 (1)	**15** (1)
Total	**233** (62)	**202** (31)†	**435** (42)

*Data are given as the number (percentage) of patients. Some patients had more than 1 complication.

†$P<.05$ vs aortic procedures.

more complications. Pulmonary complications occurred in 21% of the patients, cardiac complications occurred in 13%, and other complications occurred in 9% for an overall incidence of 42%. Respiratory failure was the single most frequent complication, occurring in 123 patients (12%). Patients with aortic conditions had a significantly higher incidence of complications compared with patients who did not have aortic conditions (Table 2). Hypotension, respiratory failure, and congestive heart failure were more frequent in patients with aortic conditions. Overall, 60% of the complications occurred during the first 3 days after the operation.

There were specific temporal patterns related to the different complications (**Table 3**). The greatest risk of hypotension (43%), MI (47%), and respiratory depression (55%) was within 1 day. The highest incidence of respiratory failure (76%), pulmonary embolus (50%), and congestive heart failure (CHF) (46%) occurred between 1 and 3 days. Pneumonia (38%) was more common between 4 and 7 days. Sepsis (71%) and cerebrovascular accident (CVA) (53%) occurred preponderantly between 8 and 30 days. Angina was diagnosed throughout the first 7 days. Renal failure had a bimodal distribution with increased frequency between 1 and 3 days (31%) and 8 and 30 days (56%). The risk of cardiac arrhythmia and gastrointestinal tract bleeding was similar throughout all intervals. These patterns were similar for aortic and nonaortic procedures (**Table 4**).

Overall there were 37 deaths (4%) in the first 30 days after the operation. Eleven (30%) were related to cardiac events. Both diagnosed pulmonary emboli were fatal. Other deaths were related to sepsis, hemorrhage, respiratory failure, or other causes. There were 9 deaths (2%) in patients with aortic conditions and 28 deaths (4%) in patients with nonaortic conditions. Overall 3 deaths (8%) occurred within 1 day, 3 (8%) between 1 and 3 days, 4 (11%) between 4 and 7 days, and 27 (73%) between 8 and 30 days. Deaths were significantly more likely to occur within the first 7 days in patients with aortic conditions compared with those who had nonaortic conditions (55% vs 18%, $P<.02$). Six (75%) of 8 deaths in the aortic group were related to cardiac events compared with 5 (17%) of 29 deaths that occurred after nonaortic procedures ($P<.001$).

Reoperation for complications was required in 71 (7%) of 1021 patients. Reoperation was more likely in patients undergoing aortic compared with nonaortic procedures (9% vs 6%, $P<.001$). These procedures were primarily for vascular occlusion, intra-abdominal infections, and intra-abdominal hemorrhage. Forty-seven percent of these procedures were undertaken more than 7 days after the index operation. This finding was similar in both groups of patients with aortic and nonaortic conditions (44% and 49%, respectively). However, patients with aortic conditions were more likely to undergo reoperations within the first 24 hours (35% vs 14%, $P<.02$).

COMMENT

Our patient population had an overall major complication rate of 42% and mortality rate of 4% within the first 30 days of operation. There are several potential explanations for this significant incidence of adverse events. The reported incidence of postoperative complications is influenced by the preoperative status of the patient, operation performed, which complications are identified, and criteria for diagnosis. This was a group of high-risk patients, having an ASA classification of III or IV, and thus were known to be at high risk for postoperative complications.[6] The patients studied were primarily older men undergoing major intra-abdominal pro-

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Table 3. Temporal Occurrence of Complications for the Total Group*

Variable	Specific Interval			
	Day 1	Days 1-3	Days 4-7	Days 8-30
Cardiac				
Myocardial infarction	21 (47)	17 (38)	5 (11)	2 (4)
Congestive heart failure	6 (17)	16 (46)	6 (17)	7 (20)
Hypotension	13 (43)	5 (17)	4 (13)	8 (27)
Cardiac arrhythmia	7 (33)	7 (33)	3 (14)	4 (19)
Angina	1 (20)	2 (40)	2 (40)	0
Pulmonary				
Respiratory failure	8 (7)	94 (76)	9 (7)	12 (10)
Pneumonia	2 (29)	24 (35)	26 (38)	16 (24)
Respiratory depression	11 (55)	2 (10)	2 (10)	5 (25)
Pulmonary embolus	0	1 (50)	1 (50)	0
Other				
Sepsis	0	4 (11)	7 (18)	27 (71)
Renal failure	2 (13)	5 (31)	0	9 (56)
Cardiovascular accident	0	4 (24)	4 (24)	9 (52)
Gastrointestinal tract bleeding	3 (20)	4 (27)	3 (20)	5 (33)
Total	**74** (17)	**185** (43)	**72** (17)	**104** (24)

*Data are given as the number (percentage) of patients. A patient may have experienced the same or another complication in more than 1 period.

cedures. We included only certain major, primarily extra-abdominal complications. Fairly strict criteria were used, however. For example, respiratory depression was defined as a $PaCO_2$ exceeding 60 mm Hg that required treatment, a situation which might not be included as a complication in many studies. Routine monitoring using an electrocardiogram and cardiac enzyme levels would detect more instances of myocardial ischemia. Conversely, these were elective procedures in patients without recent known MI, operation, or immunosuppressive therapy. Finally, different anesthetic and analgesic techniques were used as part of the main randomized study.[5] While the use of epidural anesthesia and analgesia did not improve outcome in the group as a whole, outcome was improved in patients with vascular conditions. However, our scheme of adaptive randomization would have controlled for this factor in this study. Thus, several aspects of the study design might have influenced the incidence and timing of postoperative complications.

The overall incidence of significant cardiac events diagnosed in the present study was 13%. More than two thirds of our patients had preoperative characteristics of previous cardiac disease or risk factors. This incidence is similar to other reports in high-risk patients.[7-8] For example, Mangano et al[7] reported that 18% of high-risk patients undergoing noncardiac surgery had cardiac events. Our postoperative protocol focused primarily on ischemic events and only severe arrhythmias were included.

Myocardial infarction was the most frequent cardiac complication and was diagnosed in 45 patients (4%). Almost half occurred within the first 24 hours and 85% within 72 hours of operation. This high early incidence may, in part, be because of our monitoring protocol. Patients were routinely studied using electrocardiographic monitoring and cardiac enzyme levels during this period, whereas only symptomatic MI was diagnosed later. Gedebou et al[9] found that 56% of perioperative MI occurred within 24 hours; Von Knorring[10] similarly reported that 85% of MI occurred within 72 hours. Mangano et al[7] found that half of the ischemic complications occurred by the third postoperative day and further observed that MI in the early postoperative period was more likely to be fatal. Furthermore, Charlson et al[11] used electrocardiographic and creatine phosphokinase level monitoring for 7 days and found a similar incidence of MI. New-onset angina was diagnosed in only 5 patients (1%). The incidence of these complications will depend on how they are defined and diagnosed. Since many MIs are asymptomatic and potentially lethal in the early postoperative period, high-risk patients should be monitored closely during this period.[7] The benefit of perioperative β-blockers to reduce ischemic events has been clearly established after our study was designed and implemented.[12] The use of these agents was not routine and was not monitored during the study. Thus, this might have further potential therapeutic advantage.

Congestive heart failure was diagnosed in 35 patients (3%) in the present study, Charlson et al[8] reported an incidence of 6% using diagnostic criteria similar to ours. Whereas they found that 40% of the patients had CHF diagnosed on the first day and 100% within 3 days, we found that 63% of patients had CHF diagnosed within 3 days but that patients remained at risk up to 30 days after the operation. Mangano et al[7] also found that half of the patients developing CHF presented after 3 days. Both preexisting cardiac disease and perioperative fluid management are important risk factors contributing to CHF.[8] These findings suggest that high-risk patients should be monitored most closely in the early postoperative period. As noted previously, central venous pressure was measured in 56% and Swann-Ganz catheters were used in 41% of patients overall in the present study.[5] However, routine use of Swann-Ganz catheters in particular does not clearly improve perioperative outcome.[13]

Cardiac arrhythmia (ventricular tachycardia and aterioventricular block requiring pacemaker therapy) occurred in 21 (2%) of our patients. Two thirds occurred during the first 3 days, but these events occurred through-

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Table 4. Temporal Occurrence of Complications for Patients Who Underwent Aortic and Nonaortic Procedures*

Variable	Specific Interval			
	Day 1	Days 1-3	Days 4-7	Days 8-30
Aortic Procedure Group				
Cardiac				
Myocardial infarction	9 (45)	8 (40)	3 (15)	0
Congestive heart failure	4 (17)	11 (48)	3 (13)	5 (22)
Hypotension	8 (47)	3 (18)	1 (6)	5 (29)
Cardiac arrhythmia	4 (36)	3 (27)	2 (18)	2 (18)
Angina	1 (25)	1 (25)	2 (50)	0
Pulmonary				
Respiratory failure	3 (4)	66 (84)	6 (8)	4 (5)
Pneumonia	1 (4)	11 (41)	11 (41)	4 (15)
Respiratory depression	4 (50)	1 (13)	1 (13)	2 (25)
Pulmonary embolus	0	1 (50)	1 (50)	0
Other				
Sepsis	0	1 (6)	2 (13)	13 (81)
Renal failure	2 (22)	3 (33)	0	4 (44)
Cardiovascular accident	0	4 (40)	2 (20)	4 (40)
Gastrointestinal tract bleeding	2 (29)	2 (29)	1 (14)	2 (29)
Total	**38** (16)	**115** (49)	**35** (15)	**45** (19)
Nonaortic Procedure Group				
Cardiac				
Myocardial infarction	12 (48)	9 (36)	2 (8)	2 (8)
Congestive heart failure	2 (17)	5 (42)	3 (25)	2 (17)
Hypotension	5 (38)	2 (15)	3 (23)	3 (23)
Cardiac arrhythmia	3 (30)	4 (40)	1 (10)	2 (20)
Angina	0	1 (100)	0	0
Pulmonary				
Respiratory failure	5 (11)	28 (64)	3 (7)	8 (18)
Pneumonia	1 (2)	13 (32)	15 (37)	12 (29)
Respiratory depression	7 (58)	1 (8)	1 (8)	3 (25)
Pulmonary embolus	0	0	0	0
Other				
Sepsis	0	3 (14)	5 (23)	14 (64)
Renal failure	0	2 (29)	0	5 (71)
Cardiovascular accident	0	0	2 (29)	5 (71)
Gastrointestinal tract bleeding	1 (13)	2 (25)	2 (20)	3 (37)
Total	**36** (18)	**70** (35)	**37** (18)	**59** (29)

*Data are given as the number (percentage) of patients. A patient may have experienced the same or another complication in more than 1 period.

out the postoperative period. Mangano et al[7] found that ventricular tachycardia was their most frequent cardiac complication and that most of these occurred within 3 days. We did not record other arrhythmias, but Valentine et al[14] found that atrial fibrillation occurred frequently (10%) during the first few days after aortic procedures. This increased rate of arrhythmias early postoperatively may be related to hypoxia, fluid balance, and myocardial ischemia during this period.[15] Cardiac monitoring and optimization of these factors should, therefore, be carried out in the early postoperative period in patients at risk for ventricular arrhythmia. The value of routine supplemental oxygen to prevent hypoxia, for example, might merit further investigation.

Overall, respiratory complications occurred in 20% of our patients. Similarly, Velanovich[3] reported a 15% incidence of respiratory complications in 520 patients undergoing elective procedures. The incidence varies widely, however, depending on the operation performed and how the complications are defined. While atelectasis is a frequently diagnosed complication, it was not included as such in our study.[16,17] Our focus was primarily on major respiratory complications.

Respiratory failure was the most frequently diagnosed pulmonary complication in our study. This occurred most frequently between 1 and 3 days after the operation and was primarily diagnosed because of the need for prolonged mechanical ventilatory assistance. Respiratory depression occurred more frequently within 24 hours of the operation. This may have been related to increased use of analgesics during the immediate postoperative period. We found in the main randomized study that epidural analgesia significantly reduced the incidence of respiratory failure in patients with aortic conditions ($P<.01$) and had a tendency to do so in the overall group ($P=.06$).[5]

Postoperative pneumonia occurred in 7% of our patients. The incidence of postoperative pneumonia varies from 2% to 18% in other articles.[17-20] Multiple factors seem to be involved, including aspiration, prolonged atelectasis, preoperative pulmonary status, and the need for mechanical ventilatory assistance.[16-20] Pneumonia was diag-

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nosed throughout the postoperative period in our study. Using diagnostic criteria similar to ours, Ephgrave et al[19] found pneumonia occurring in 5% of patients at 1 day, 12% between 1 and 3 days, 41% between 4 and 7days, and 31% between 8 and 30 days. Several strategies should be considered to reduce this complication. Techniques to improve pulmonary hygiene, such as deep breathing, coughing, and forced expiration, seem to reduce the incidence of pneumonia and atelectasis.[16] The benefit of improved analgesia on this complication is less clear.[5,17]

Renal failure occurred in 16 patients (2%) and had a bimodal distribution with 44% occurring within 3 days and the other 56% 7 days after the operation. Charlson et al[21] found that 23% of their patients had a 20% increase in their serum creatinine levels within 7 days and that most developed impaired renal function within the first 24 hours. However, we used stricter criteria to diagnose renal failure in our study. Renal failure in the early postoperative period is usually due to either prerenal or postrenal factors. The later occurrence may reflect intrinsic renal damage caused by the toxic effects of a drug. Renal failure is an important predictor of postoperative mortality.[4] Since the diagnosis is generally straightforward, emphasis should be placed on prevention during the postoperative period.

We found a 4% mortality rate within 30 days of operation. About 75% of the deaths occurred beyond the first postoperative week. Browner et al[4] found that about 50% of the postoperative deaths occurred more than 3 weeks after the operation. Thirty percent of our deaths were cardiac related. Browner et al[4] found that only one fourth of the deaths in their study were related to cardiac events even in patients at high risk for cardiac complications. In both our study and theirs, sepsis and other organ failure were important determinants of postoperative death. Most of the suggested strategies to prevent complications use interventions in the immediate postoperative period. Whether such interventions would reduce the mortality, particularly those occurring later in the postoperative period, remains speculative and requires further investigation.

Reoperation for complications was required in 7% of the cases. This incidence is similar to that reported by others.[22-24] Such procedures were primarily required for intra-abdominal complications such as hemorrhage and infection rather than for the other extra-abdominal complications. Half of our reoperations were performed more than 7 days after the operation. Harbrecht et al[22] found that relaparotomy was performed within the first week for hemorrhage and dehiscence and later for other causes such as infection, obstruction, and ischemia. Relaparotomy is associated with a 50% mortality rate.[22-24]

We compared patients undergoing aortic procedures with those undergoing nonaortic procedures to determine whether the type of operation might influence the temporal patterns of complications. Aortic procedures were associated with a higher incidence of complications and death. Deaths were more likely to occur within the first postoperative week in patients undergoing an aortic procedure, as was the need for reoperation. However, the temporal patterns of occurrence of specific complications was similar in both groups.

While major complications occur throughout the postoperative period, the greatest incidence is 1 to 3 days after the operation. However, specific complications have different temporal patterns of occurrence: early postoperative, several days after the operation, throughout the postoperative period, and in the late postoperative period. Knowledge and appreciation of these patterns will enhance clinical management and should form the basis for future interventional trials.

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REFERENCES

1. Collins TC, Daley J, Henderson WH, Khuri SF. Risk factors for prolonged length of stay after major elective surgery. *Ann Surg.* 1999;230:251-259.
2. Meguid MM, Debonis D, Meguid V, Hill LR, Terz JJ. Complications of abdominal operations for malignant disease. *Am J Surg.* 1988;156:341-345.
3. Velanovich V. The value of routine preoperative laboratory testing in predicting postoperative complications: a multivariate analysis. *Surgery.* 1991;109:236-243.
4. Browner WS, Li J, Mangano DT, for the Study of Perioperative Ischemia Research Group. In-hospital and long-term mortality in male veterans following noncardiac surgery. *JAMA.* 1992;268:228-232.
5. Park WY, Thompson JS, Lee KK. Effect of epidural anesthesia and analgesia in perioperative outcome: a randomized, controlled Veterans Affairs Cooperative Trial. *Ann Surg.* 2001;234:560-571.
6. Dripps RD, Lamont A, Eckenhoff JE. The role of anesthesia in surgical mortality. *JAMA.* 1961;178:261-266.
7. Mangano DT, Browner WS, Hollenberg M, London MJ, Tubau JF, Tateo IM, for the Study of Perioperative Ischemia Research Group. Association of perioperative myocardial ischemia with cardiac morbidity and mortality in men undergoing noncardiac surgery. *N Engl J Med.* 1990;323:1781-1788.
8. Charlson ME, MacKenzie CR, Gold JP, Ales KL, Topkins M, Shires GT. Risk for postoperative congestive heart failure. *Surg Gynecol Obstet.* 1991;172:95-104.
9. Gedebou TM, Barr ST, Hunter G, Sinha R, Rappaport W, VillaReal K. Risk factors in patients undergoing major nonvascular abdominal operations that predict perioperative myocardial infarction. *Am J Surg.* 1997;174:755-758.
10. Von Knorring J. Postoperative myocardial infarction: a prospective study in a risk group of surgical patients. *Surgery.* 1981;90:55-60.
11. Charlson ME, MacKenzie CR, Gold JP, et al. The preoperative and intraoperative hemodynamic predictors of postoperative myocardial infarction or ischemia in patients undergoing noncardiac surgery. *Ann Surg.* 1989;210:637-348.
12. Mangano DT, Layug EL, Wallace A, Tateo I. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery: multicenter study of the Perioperative Ischemia Research Group. *N Engl J Med.* 1996;335:1713-1720.
13. Barone JE, Tucker JB, Rassias D, Corvo PR. Routine perioperative pulmonary artery catheterization has no effect on rate of complications in vascular surgery: a meta-analysis. *Am Surg.* 2001;67:674-679.
14. Valentine RJ, Rosen SF, Cigarroa JE, Jackson MR, Modrall JG, Glagett GP. The clinical course of new-onset atrial fibrillation after elective aortic operations. *J Am Coll Surg.* 2001;193:499-504.
15. O'Kelly B, Browner WS, Massie B, Tubau J, Ngo L, Mangano DT, for the Study of Perioperative Ischemia Research Group. Ventricular arrhythmias in patients undergoing noncardiac surgery. *JAMA.* 1992;268:217-221.
16. Roukema JA, Carol EJ, Prins JG. The prevention of pulmonary complications after upper abdominal surgery in patients with noncompromised pulmonary status. *Arch Surg.* 1988;123:30-34.
17. Jayr C, Mollie A, Bourgain JL, et al. Postoperative pulmonary complication: gen-

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eral anesthesia with postoperative parenteral morphine compared with epidural analgesia. *Surgery.* 1988;104:57-63.
18. Fujita T, Sakurai K. Multivariate analysis of risk factors for postoperative pneumonia. *Am J Surg.* 1995;169:304-307.
19. Ephgrave KS, Kleiman-Wexler R, Pfaller M, Booth B, Werkmeister L, Young S. Postoperative pneumonia: a prospective study of risk factors and morbidity. *Surgery.* 1993;114:815-821.
20. Garibaldi RA, Britt MR, Coleman ML, Reading JC, Pace NL. Risk factors for postoperative pneumonia. *Am J Med.* 1981;70:677-680.
21. Charlson ME, MacKenzie CR, Gold JP, Shires GT. Postoperative changes in serum creatinine: when do they occur and how much is important? *Ann Surg.* 1989; 209:328-333.
22. Harbrecht PJ, Garrison RN, Fry DR. Early urgent relaparotomy. *Arch Surg.* 1984; 119:369-374.
23. Bunt TJ. Urgent relaparotomy: the high-risk, no-choice operation. *Surgery.* 1985; 98:555-560.
24. Zer M, Dux S, Dintsman M. The timing of relaparotomy and its influence on prognosis: a 10 year survey. *Am J Surg.* 1980;139:338-343.

DISCUSSION

Jack Pickleman, MD, Chicago, Ill: Thank you, President Prinz. First of all it gives me great pleasure to address you. You know you are getting old when one of your former residents sits there as president of an organization such as this, and I could not be more pleased and proud at this moment.

This is a very interesting paper. When I first read it, I sort of felt like a North Korean chef at the Westminster Dog Show. I just wanted to sit there and see more and more. But in the end, I was left with a study of complications observed in a thousand patients from 15 Veterans Affairs hospitals and therein lays the problem with this study. A major complication rate of 42% was noted. This is far in excess of usual norms for the types of operations studied, even considering the fact that only ASA III and IV male veterans were included. Is the problem the relatively small number of patients, the multiple hospital sites, or the definition of major complications? Unfortunately, from the information given, I am not sure we know, and so we have to look at the data we have and try to walk away with something clinically useful.

Some of these findings are consonant with the literature and everyday clinical experience. Hypotension and respiratory depression were more common on day 1. Respiratory failure on days 1 through 3, pneumonias on days 4 through 7, and sepsis on days 8 through 30. What was a bit surprising to me, however, was the peak incidence of myocardial infarction on day 1, common teaching being that it should occur later in the postoperative period coincident with third-space fluid resorption. If borne out by subsequent studies, all of these findings have implications for postoperative monitoring, postoperative testing, and use of intensive care unit resources.

Rather than ruminate further, I would like to ask the authors 5 specific questions. How do you explain the 42% incidence of major complications in this series? This is a figure commonly associated with more complex operations such as the Whipple procedure or, as we heard yesterday, the exact 42% incidence with right hepatic lobectomy and concomitant caval resection. Regarding your patients with pulmonary embolus [PE], you had no diagnosed nonfatal PEs which is a bit surprising, and a fatal PE rate of 0.2%, again consonant with the literature. Could you tell us something about whether these patients had routine deep vein thrombosis prophylaxis and what it was?

You compared your aortic and nonaortic operations. I would like to subdivide it a little bit further. Do the different nonaortic operations you studied, the biliary, gastric, and colonic, have different complication profiles?

Next, half of your patients received epidural anesthesia in addition to general anesthesia. Was their complication incidence or profile affected by this adjunct? And, lastly and most importantly, if you trust your own data, what changes in perioperative management do you plan to institute now?

In conclusion, this is an important paper and studies like this are going to become even more important as we strive to develop clinical pathways and replace surgical judgment and feelings with data-driven decisions. I surely appreciated reviewing the manuscript and commenting on this study.

Merrill T. Dayton, MD, Salt Lake City, Utah: I did have a couple of brief questions. First, if I understood your presentation correctly, all of these patients were ASA Class III and IV patients. Why were ASA Class I and II patients excluded? I was a little surprised to see that. Second, did your sepsis series include all wound infections? I presume that it included anastomotic leaks and abscesses, but I was interested to learn whether it was inclusive of all wound infections.

Gregory J. Jurkovich, MD, Seattle, Wash: John, I wondered if you could comment on the common causes of a postoperative fever and their timing, specifically, atelectasis, wound infection, and then urinary tract infection and deep vein thrombosis. Where did those complications fit in this timing sequence?

Jeffrey Landercasper, MD, LaCrosse, Wis: I would like to know if the rate of postoperative complication changed during the course of the study similar to other studies such as studies of postoperative infections in the Veterans Affairs system and other hospitals where if you tell a group of surgeons who are in the institution you are going to study a specific condition and complication, you can actually predict that you will change the outcome and improve the complication rates. It's been termed the "Hawthorne effect." Did you notice a change over time in your rate of complications in the study because you were studying the question?

Richard C. Thirlby, MD, Seattle: The perioperative myocardial infarction data is consistent with my bias. Dr Pickleman said that he thinks that most myocardial infarctions occur on the third day after surgery. It is my belief that the diagnosis is frequently made on the third day, but in retrospect, the myocardial infarction probably occurred in the operating room. Do you have any idea from your data what percentage of these MIs were clinically silent and diagnosed with screening electrocardiograms?

Dr Thompson: I appreciate all of the reviewers' comments. This was, as I mentioned, part of a randomized prospective study designed to look at the impact of epidural anesthesia and analgesia on surgical outcome which we have presented earlier. It was carried out at a number of Veterans Affairs medical centers so the design had several limitations. We were specifically trying to target a high-risk population so we would have a higher incidence of complications to study, and that was the reason to look at primarily ASA III and IV patients. In addition, the design limited the amount of data that were collected.

To begin with Dr Pickleman's comments, the 42% complication rate does seem high, and I think there are many explanations. The first I just mentioned. We were trying to define a high-risk group of patients who would have more complications. The complications had predefined criteria and they were studied and surveilled by independent individuals at each of the study centers so the data are real. For example, if you look at the complication respiratory depression, this was defined as a P_{CO_2} of greater than 60 in the first 24 hours, that might require Narcan (naloxone). This might not typically find its way into an outcomes paper. We sought MI by routine electrocardiographic monitoring and cardiac enzyme levels in the early postoperative period which will pick up more of these complications.

One of the other questions was about the MIs and how many were silent. I do not know the exact number, but in fact, many of these were (silent), and if you look at the literature, our incidence is very similar to others. There is a fairly high

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risk of silent MIs early postoperatively. I suspect if you are just identifying the symptomatic ones, they may occur later in the postoperative period than the group that we saw here.

Dr Pickleman asked the question about PE. I am as surprised as you are at the very low incidence. The criteria for diagnosing PE were clinical symptoms confirmed by a VQ [ventilation perfusion] scan or an arteriogram. So the criteria were fairly standard, but we did not perform aggressive surveillance in terms of ultrasonography. I suspect we missed many asymptomatic events. We did not routinely look for deep venous thrombosis in this study and so likewise we are not aware of that incidence.

It is an interesting question, should we have subdivided the gastrointestinal tract procedures out separately? I did not do that. The numbers start getting small as you see when you talk about the biliary procedures and the gastric procedures. My impression is that we would not see large differences between those groups.

As noted, the study was designed so that half of the patients would have supplemental epidural anesthesia and analgesia. We used a form of adaptive randomization in the original study so that within these groups half of the patients with aortic conditions would have been randomized to epidural anesthesia and half of the patients with colonic conditions, and so forth. Thus, the influence of that factor would have been equalized.

In the main paper we found disappointingly that the use of epidural anesthesia, if we combined all of these patients, did not have a major influence overall on the complication rate or death rate that we had speculated that it would. It would be interesting to know if epidural anesthesia changes the temporal occurrence of these complications.

What plan does this lead us to? The message is, particularly when you are looking at these different cardiac events, that you have to monitor these patients aggressively coming right out of the operating room. There was a question Dr Thirlby raised about the timing and occurrence in the operating room. There have been several good studies in the literature looking at the timing of cardiac events perioperatively. The postoperative ones probably only account for about 40% of the events. Many of them, particularly arrhythmias, occur in the operating room.

The other interesting implication of this, if you look at the bimodal distribution in the patients with renal failure, is a causative one. Most of us would feel that early-onset renal failure is probably related to prerenal factors, and perhaps postrenal factors, whereas the late occurrence could be intrinsic, for example, due to drug-induced toxic reactions. This information could help influence how you approached those problems.

Dr Dayton asked about whether the sepsis category included problems such as wound infections. It did not. By definition to be in the sepsis category you had to have a clinical picture of sepsis with positive blood cultures as well as another infection. Again, one of the limitations about designing a big trial like this is you can think of all kinds of questions you would have like to have asked or have answered, but to get the main study done required trimming back many of the aspects that we would like to have studied.

Dr Jurkovich we did not look at urinary tract infections and wound infections for that same reason.

Dr Landercasper asked about whether the incidence of these complications changed over time. We looked carefully at occurrence among the different medical centers and did not find a change. Of course, in this study we were blinded to the outcome. Thus, other than the benefit of the fact that we were looking for these things, we had no knowledge of how we were doing which might have changed our patterns at that time.

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