Preoperative Cardiac Events in Elderly Patients with Hip Fracture Randomized to Epidural or Conventional Analgesia

Idit Matot, M.D.,* Arieh Oppenheim-Eden, M.D.,† Ruand Ratrot, M.D.,‡ Julia Baranova, M.D.,‡ Elyad Davidson, M.D.,* Sharon Eylon, M.D.,§ Amos Peyser, M.D.,§ Meir Liebergall, M.D.,§

Background: Perioperative myocardial ischemia occurs in 35% of unselected elderly patients undergoing hip fracture surgery. Perioperative epidural analgesia may reduce the incidence of adverse cardiac events.

Methods: The effect of early administration of epidural analgesia during the stressful *presurgical* period, on *preoperative* cardiac events was evaluated in a prospective randomized study in 68 patients with hip fractures who either had known coronary artery disease or were at high risk for coronary artery disease. On admission to the emergency room, patients were assigned to receive a usual care analgesic regimen (intramuscular meperidine, control group, n = 34) or continuous epidural infusion of local anesthetic and opioid (epidural group, n = 34). Monitoring in the preoperative period included a preoperative history and physical examination, daily assessment of cardiac adverse events, serial electrocardiograms, cardiac enzymes, and pain scores.

Results: Preoperative adverse cardiac events were significantly more prevalent in the control group compared with the epidural group (7 of 34 *vs.* 0 of 34; *P* = 0.01). Adverse cardiac events included fatal myocardial infarction in three, fatal congestive heart failure in one, nonfatal congestive heart failure in one, and new onset atrial fibrillation in two. The incidence of intraoperative and postoperative adverse cardiac events was similar for the two groups. The significant difference between groups in the incidence of preoperative cardiac events prompted interruption of the study after the planned interim analysis.

Conclusions: The authors' data indicate that compared with conventional analgesia, early administration of continuous epidural analgesia is associated with a lower incidence of preoperative adverse cardiac events in elderly patients with hip fracture who have or are at risk for coronary artery disease. Preoperative epidural analgesia may be advantageous for this surgical population.

THE worldwide prevalence of hip fracture is increasing considerably, and it is predicted to triple relative to current rates by the year 2030–2050.[1,2] Since hip frac-

This article is featured in "This Month in Anesthesiology." Please see this issue of ANESTHESIOLOGY, page 6A.

* Staff Anesthesiologist, ‡ Resident in Anesthesiology, Department of Anesthesiology and Critical Care Medicine, § Staff Orthopedic Surgeon, Department of Orthopedic Surgery, Hadassah Hebrew University Medical Center. † Staff Anesthesiologist, Department of Anesthesiology and Critical Care Medicine, Lady-Davis Medical Center, Haifa, Israel.

Address reprint requests to Dr. Matot: Department of Anesthesia and Critical Care Medicine, Hadassah University Medical Center, POB 12000, Jerusalem 91120, Israel. Address electronic mail to: matoth@cc.huji.ac.il. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

tures occur predominantly in elderly patients, a large prevalence of underlying coronary artery disease (CAD) might be expected.[3,4] The overall incidence of perioperative myocardial ischemia in elderly patients undergoing hip fracture surgery has been reported to be 35–42%.[5,6,7] Previous studies[8-12] indicated that the principal causes of in-hospital death after hip fracture were cardiac failure and myocardial infarction, which occurred early after the fracture, peaking at 2 days; bronchopneumonia, which accounted for the majority of late deaths; and pulmonary embolism, which peaked in the second week after injury. In addition, an increased risk of in-hospital mortality was found among patients with hip fracture and concomitant cardiac disease.[8] Whereas early surgical intervention, early mobilization, antibiotics, and prophylactic anticoagulation reduced death from bronchopneumonia and pulmonary embolism after hip fracture,[9,12] only few interventions have been made in this patient population to reduce death from cardiac failure or myocardial infarction.

Recent research on prevention of perioperative cardiac morbidity and mortality has focused on modulating sympathetic response with the perioperative use of β blockers[13-15] or α_2 agonists.[16-17] In recent years, epidural analgesia has been shown to exert a favorable effect on the stress response.[18] In addition to providing sympatholysis, local anesthetics also relieve pain, which is a potent trigger for the stress response. Yeager *et al.*[19] reported that compared to standard nonepidural analgesic technique, epidural analgesia reduced the incidence of postoperative cardiac complications in a group of high-risk patients scheduled for noncardiac surgery. Therefore, we hypothesized that the use of epidural analgesia during the stressful *presurgical* period would decrease the incidence of adverse cardiac events in patients with fractured hips. We conducted a randomized clinical trial in elderly patients with or at risk for CAD who had sustained a traumatic hip fracture, comparing preoperative epidural (local anesthetic and opioid) to conventional (intramuscular opioid) analgesia with respect to preoperative cardiac events.

Materials and Methods

Patients

The trial was approved and monitored by the Research Ethics Committee of the Hadassah University Medical Center (Jerusalem, Israel), and written, informed consent was obtained from each patient. Successive patients aged 60 yr or older who presented to the emergency

department of Hadassah University Medical Center with a traumatic hip fracture, were able to sign informed consent, and had either known CAD (as indicated by previous myocardial infarction, typical angina, atypical angina with positive stress test results, or angiographic or scintigraphic evidence of CAD), or were at high risk for CAD (the patient had at least two of the following cardiac risk factors: age $\geq$ 65, hypertension, current smoking, serum cholesterol level > 240 mg/dl, and diabetes mellitus)[13,14] were studied prospectively during a 12-month period (October 1998–September 1999). Patients were excluded from the study in the presence of contraindications to epidural analgesia, known allergy to any of the study drugs, acute coronary insufficiency, electrocardiographic evidence of left bundle branch block, or 10 h or more from the time of injury.

Design and Procedures

On admission to the emergency room, patients who met inclusion criteria were randomly assigned by the attending anesthesiologist and orthopedic surgeon, by random numbers, to one of two groups. Patients in the control group (n = 34) received standard pain relief regimen, specifically 1 mg/kg intramuscular meperidine every 6 h. Oral or intramuscular dipyrone was given when pain relief was inadequate (visual analog scale score > 30 mm). In patients randomized to epidural analgesia (epidural group, n = 34), an epidural catheter was inserted into the lumbar epidural space at the L2–L3 or L3–L4 interspace. A 3-ml test dose of 2% lidocaine with epinephrine (1:200,000) was then administered. Pain relief was provided with 4 mg methadone and 7–10 ml bupivacaine, 0.25%, followed by a continuous epidural infusion of 16 mg methadone and 45 mg bupivacaine (0.5%) over 24 h. Epidural bupivacaine (0.25%, 5 ml) was administered when pain relief was inadequate (visual analog scale score > 30 mm). All patients in both groups received oxygen by nasal cannulae (7 l/min), and preoperative fluid administration was monitored.

On admission to the emergency room, a detailed history was obtained, a physical examination was performed, and all cardiovascular medications were recorded. Electrocardiography, standard biochemical and hematologic tests, and serum cardiac enzyme concentrations (creatine kinase [CK] and CK-MB isoenzyme, troponin-T) were determined. The above mentioned measurements were routinely determined and reviewed upon admission to the orthopedic ward, daily during the preoperative period, before surgery, postoperatively in the recovery room and daily until the third postoperative day, and on the day of discharge. Additional CK, CK-MB, and troponin-T samples were drawn when clinically indicated or when electrocardiographic changes suggested myocardial infarct. Pain scores, measured on a 0- to 100-mm (0 = no pain) visual analog scale score for pain, with the patient resting and while slightly moving

the fractured leg, were also obtained before and 1 h after administration of analgesia, every 6 h during the preoperative period, before surgery, and every morning until discharge.

All cardiac medications were continued until surgery. The anesthetic technique and the amount of anesthetics administered were chosen by the anesthesiologist caring for the patient. After surgery, patients were transferred to the recovery room where they stayed for at least 3 h. Epidural analgesia was continued postoperatively, and the decision to change to oral analgesics was left to the discretion of the pain service team. Patients received enoxaparin sq (40 mg) once daily, starting after surgery. During hospitalization, all patients were examined and interviewed daily. Adverse outcomes, which were detected by the examining physician, were validated by two of the other investigators who were not aware of the patient's pain reduction regimen.

Study End Points

The primary end point of the study combined cardiac death, myocardial infarction, unstable angina, congestive heart failure (CHF), and new-onset atrial fibrillation in the preoperative period. The cardiac events were defined to be comparable with those used by Mangano *et al.*[13,14,16,20]: Diagnosis of myocardial infarction required (1) an elevation of the CK-MB isoenzyme or troponin-T concentration above the hospital laboratory's myocardial infarction threshold and (2) either new Q waves (duration $\geq$ 0.03 s) or persistent changes (4 days) in ST-T segment. Unstable angina was defined as severe precordial chest pain that lasted 30 min or more and was unresponsive to standard therapeutic maneuvers, associated with ST-segment or T-wave changes without the development of Q waves or cardiac enzyme abnormalities. CHF was defined by clinical (shortness of breath, rales, jugular venous distention, peripheral edema, third heart sound) and radiologic (cardiomegaly, interstitial edema, alveolar edema) signs that required a change in medication involving at least treatment with diuretic drugs. New atrial fibrillation required 12-lead electrocardiographic confirmation. Cardiac death was defined as death due to myocardial infarct, CHF, or arrhythmia. Analyses were by intention to treat.

Although our primary objective was to determine whether there is a difference in adverse cardiac events in the preoperative period, we also examined postoperative complications. Three main protocol-defined secondary end points were monitored: (1) cardiac events; (2) pulmonary embolism (as evidenced by spiral computed tomography scanning); and (3) pneumonia (new infiltrate on chest x-ray combined with two of the following: temperature higher than 38°C, leukocytosis, positive sputum culture). Chest x-ray and spiral computed tomography were performed only when clinically indicated.
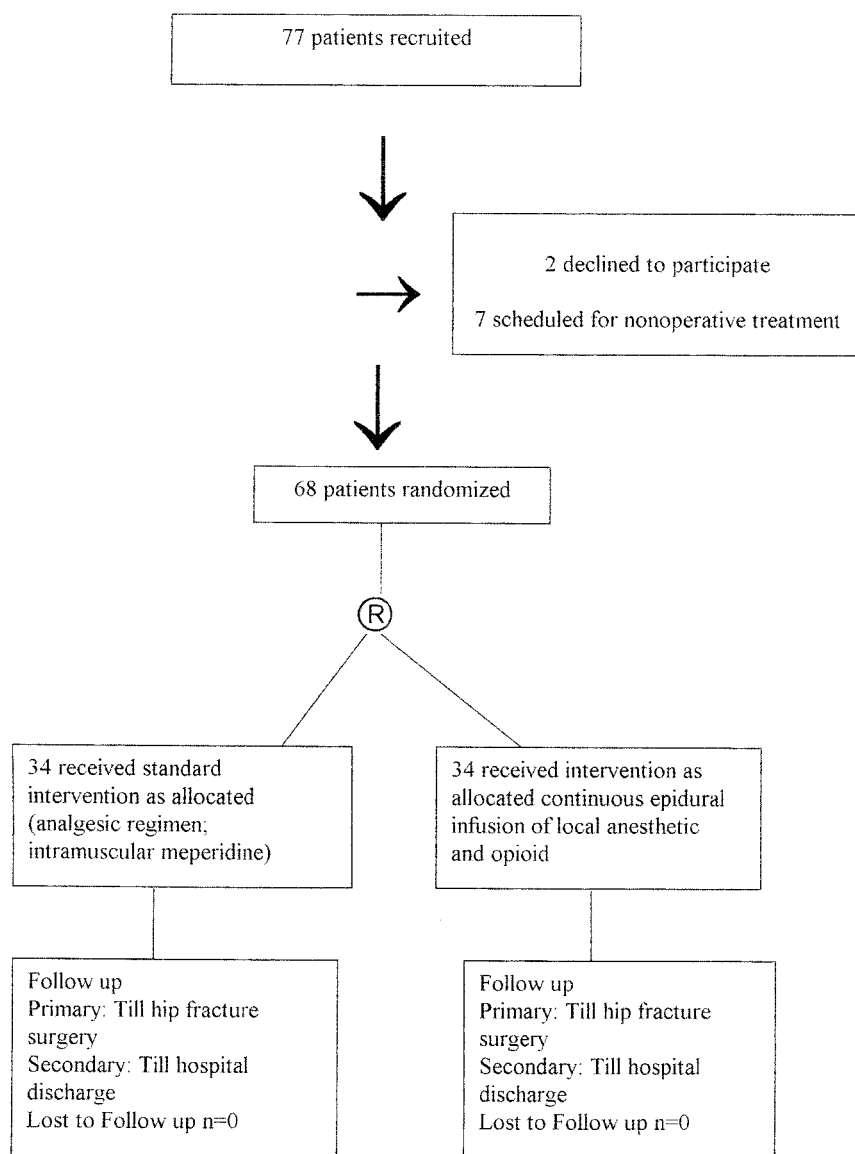
Fig. 1. Trial profile.

Statistics

A power analysis for adverse cardiac events as an outcome, with 80% power to detect a 25% reduction in this outcome and significance of 0.05 or less, assuming 15% incidence of major cardiac morbidity or death, indicated that 160 patients were required in each group. As part of the study design, an interim analysis by an independent safety committee was planned after 1 yr. In accordance with the Fleming-Harrington-O'Brien criteria,[21] the protocol specified that the trial would be stopped if there was a significant difference in the rate of the primary end point between the two groups ($P <$ 0.015).

Categorical data were analyzed using the chi-square test or Fisher exact test. Differences between the means of two groups were compared using the Student t test. Mortality and morbidity in the two groups were compared using the Fisher exact test. Analysis was per-formed using Statistical Analysis System software (version 6.12; SAS Institute, Cary, NC). Results are expressed as mean $\pm$ SD.

Results

The study was terminated at the time of the interim analysis. A total of 77 elderly patients with traumatic hip fracture who fulfilled entry criteria were admitted to Hadassah Hospital Medical Center over a period of 12 months (fig. 1). Among them, nine (12%) were not included in the study because of patient refusal (two patients, 2.5%) or because they were scheduled for non-operative treatment due to nonambulatory status prefracture (seven patients, 9%). Of the remaining 68 patients, 34 were randomized to conventional analgesia (control group), and 34 were randomized to epidural analgesia. The mean ages were 81.4 $\pm$ 8.1 and 81.0 $\pm$

Table 1. Patient Characteristics

	Control Group (n = 34)	Epidural Group (n = 34)
Sex (male/female)	7/27	6/28
Age (yr)	81.4 ± 8.1	81.0 ± 8.1
Weight (kg)	64.2 ± 11.5	60.1 ± 8.6
Height (cm)	163 ± 8	161 ± 7
ASA II/III	18/16	17/17
Definite CAD, n	14	16
Previous myocardial infarction, n (%)	6 (43)	7 (44)
Typical angina, n (%)	9 (64)	11 (69)
Previous coronary bypass, n (%)	3 (21)	4 (24)
Previous PTCA, n (%)	1 (7)	1 (6)
History of CHF, n (%)	3 (21)	2 (12)
Risk factors for CAD, n	20	18
Age, 65 yr, n (%)	20 (100)	18 (100)
Hypertension, n (%)	15 (75)	14 (78)
Current smoking, n (%)	2 (10)	3 (16)
Cholesterol, 240 mg/dl, n (%)	3 (15)	3 (16)
Diabetes mellitus, n (%)*	4 (20)	4 (22)
Cardiac medications		
β-Adrenergic blocker, n (%)	16 (47)	18 (53)
Calcium channel blocker, n (%)	5 (15)	2 (8)
Diuretics, n (%)	10 (30)	13 (38)
Nitrates, n (%)	7 (21)	5 (15)
ACE inhibitors, n (%)	6 (18)	6 (18)

Values are mean ± SD. There were no significant differences between the groups.

* All patients had type II diabetes mellitus.

ACE = angiotensin converting enzyme; CAD = coronary artery disease; CHF = congestive heart failure; PTCA = percutaneous transluminal coronary angioplasty.

8.1 yr, and 79% and 82% were women in the control and epidural groups, respectively. Demographic data and information on concomitant medical conditions, time to repair, surgical procedures, and anesthetic technique are listed in tables 1 and 2. Randomization was successful in achieving comparable groups for all characteristics listed, including sex, age, weight, height, American Society of Anesthesiologists (ASA) physical status, percentage of patients with CAD or with risk factors for CAD, and cardiac medications. The time from admission to the emergency room to surgery ranged between 4 and 54 h and was not significantly different among the groups. A similar volume of fluid was administered in the preoperative period to patients in both groups.

Primary Outcomes: Preoperative Period

Preoperative adverse cardiac events were significantly more prevalent in the control group compared with the epidural group: seven patients in the control group (20%), as compared with no patient in the epidural group ($P = 0.01$, table 3). Adverse cardiac events in these seven patients included fatal myocardial infarction in three, fatal CHF in one, nonfatal CHF in one, and new onset atrial fibrillation in two. All occurred in the preoperative period, while the patients were waiting in the orthopedic department for their surgery. Of the seven episodes, only three were recognized clinically: one of the three fatal myocardial infarctions and all CHF events. In two control group patients, a 12-lead electrocardio-

Table 2. Characteristics of Perioperative Clinical Data

	Control Group (n = 34)	Epidural Group (n = 34)
Time from fall to emergency room arrival (h)	4.18 ± 2.21	4.38 ± 2.5
Time from emergency room to surgery (h)	28.6 ± 18.2*	25.9 ± 16.7
Duration of operation (min)	86.5 ± 33.7*	85.6 ± 28
Anesthetic technique (n)		
Epidural anesthesia	0*	30
Spinal anesthesia	27*	0
General anesthesia	3*	4†
Surgical procedure (n)		
Dynamic hip screw and plate fixation	17	20
Hemiarthroplasty	11	12
Cannulated hip screw	2	2

* n = 30; four patients died in the preoperative period. † These patients received combined general–epidural anesthesia.

Table 3. Outcomes by Type of Analgesia Received

Outcome	Control	Epidural
Primary outcome, total patients (n)	34	34
Preoperative cardiac events	7* (20)	0
Congestive heart failure	1 (2.9)	0
New onset atrial fibrillation	2 (5.9)	0
Death	4 (11.7)	0
Secondary outcome, total patients (n)	30	34
Postoperative cardiac events	4 (13.3)	2 (5.9)
Myocardial infarction	1 (3.3)	1 (2.9)
Congestive heart failure	0	1 (2.9)
New onset atrial fibrillation	3 (10)	0
Postoperative noncardiac events		
Bronchopneumonia	2 (6.6)	2 (5.9)
Pulmonary embolism	1 (3.3)	1 (2.9)

Percentages are given in parentheses.

* $P = 0.011$.

graph and elevation in cardiac enzymes confirmed the diagnosis of acute myocardial infarction, and in the remaining two, new atrial fibrillation was present. There were no deaths from other causes. Two of these patients received β-adrenergic blockers. In separate analysis, patients with cardiac events had a significantly higher percentage of male gender, ASA physical status III, and established CAD compared to those without such events (table 4). Their ages and weights were not significantly different from the other patients. In the four patients who died in the preoperative period (table 5), signs of adverse cardiac event developed 20 ± 4 h after admission to the emergency room, and death occurred 204 ± 278 h (range, 40 h–26 days) after diagnosis.

In both groups, pain scores at rest were significantly lower after 1 h of analgesia than before the administration of analgesia (fig. 2). No differences in pain scores at rest were found between groups before surgery. Pain scores, however, were significantly higher in the control group when the patients were asked to move the fractured leg slightly.

Secondary Outcomes: Postoperative Period

Table 2 shows that, with the exception of the type of anesthesia administered, the groups were similar with

Table 4. Characteristics of Patients with Preoperative Cardiac Events

	Patients with Cardiac Events (n = 7)	Patients without Cardiac Events (n = 61)
Men, % (n)	71 (5)*	13 (8)
ASA physical status III, % (n)	100 (7)*	43 (26)
Known CAD, % (n)	86 (6)*	39 (24)
Age (yr)	80.5 ± 9.8	81.9 ± 8.7
Weight (kg)	66.2 ± 11.6	63.3 ± 9.8

There were no significant differences between the groups in age and height, and there were significant differences in the percentage of patients with male gender, ASA III physical status and known CAD.

* $P < 0.05$ compared with the other group.

CAD = coronary artery disease.

regard to the mix of surgical procedures and the duration of the operation. The median duration of epidural analgesia was 2 days. In the first 2 postoperative days, pain scores were significantly higher in the control group compared to the epidural group (data not shown). No differences in pain scores were found from the third postoperative day until discharge.

The incidence of intraoperative and postoperative adverse cardiac and noncardiac events was similar for the two groups (table 3). However, when the entire perioperative period is tested, the incidence of perioperative adverse cardiac events was significantly higher in the control group compared with the epidural group (11 of 34 *vs.* 2 of 34).

Postoperatively, two patients had myocardial infarction (one in each group), three patients suffered from new onset atrial fibrillation (all from control group), one patient had CHF (epidural group), four patients had bronchopneumonia (two from each group), and one patient had pulmonary embolism (control group).

Discussion

The major finding of this study was that the incidence of adverse cardiac events in the preoperative period in high-risk patients with fractured hip was higher in patients randomized to receive conventional (intramuscular opioid) analgesia than in those randomized to receive epidural analgesia. The combined incidence of these cardiac events was 20% in the control group, as compared with none in the epidural group. Our study extends preliminary work of Scheinin *et al.*,[6] who demonstrated that perioperative analgesic management with continuous epidural analgesia, started preoperatively, reduced the amount of myocardial ischemia in elderly patients with hip fractures. In contrast to our study, however, an unselected group of patients was included in that study, cardiac enzymes were not measured, and the study end point did not include clinically relevant adverse cardiac events, such as CHF or unstable angina.[6] Also, the lower number of males in the control group, as the authors suggested, may have obscured possible trends.

At first glance, the overall incidence of death (four patients, 5.8%) reported here seems high. However, this event rate is consistent with earlier studies that reported in-hospital mortality rates ranging from 1.4% to 12% in unselected groups of patients with hip fractures.[4,8–11,22–26] In the early 1970s,[10,11] the reported causes of in-hospital death were bronchopneumonia (25–49%), pulmonary embolism (12–19%), and cardiac events (12–16%). Perez *et al.*,[9] who reviewed consecutive autopsy reports of 581 patients with hip fracture, found that the majority of in-hospital deaths were due to bronchopneumonia (46%), cardiac events (23%) and pulmonary embolism

Table 5. Details of Patients Who Died in the Preoperative Period

	Patient			
	1	2	3	4
Sex	Male	Male	Male	Male
Age (yr)	80	91	85	79
Concomitant diseases	Hypertension, CAD (previous PTCA, angina pectoris)	Diabetes, CAD (previous MI, history of CHF)	Diabetes, hypertension, CAD (previous MI, previous coronary bypass)	Hypertension, CAD (angina pectoris, history of CHF)
Cardiac event	MI	MI	MI	CHF
Presenting sign	Chest pain	12-lead ECG and elevation in cardiac enzymes	12-lead ECG and elevation in cardiac enzymes	Overt pulmonary edema
In-hospital course	Fatal arrhythmias developed	While recovering from MI, patient's subsequent course was complicated by pneumonia from which he did not recover	The patient underwent successful PTCA. Two days later was found in bed confused with cyanosis, tachypnea, and right-sided lung infiltrate, suggesting aspiration. The patient was intubated and underwent ventilation. Multiorgan failure developed later.	Patient was intubated and underwent ventilation. CHF did not improve with medical treatment

CAD = coronary artery disease; CHF = congestive heart failure; ECG = electrocardiography; MI = myocardial infarct; PTCA = percutaneous transluminal coronary angioplasty.

(14%). These authors noted that death from cardiac origin occurred early after fracture, peaking at 2 days after injury. Sutcliffe et al.[25] also found bronchopneumonia (30%) and cardiac events (23%) to account for the majority of deaths in 1,333 patients who underwent surgical repair of a hip fracture. In the 1990s, three studies[23,24,26] reported a decline in death from bronchopneumonia, with cardiac events as the principal cause of death (35–63%) in an unselected group of patients presenting with fractured femur. Our results in the high-risk patients are therefore consistent with these observations in an unselected group of patients presenting with hip fracture.

Previous studies[3,13,21] evaluating perioperative cardiac morbidity and mortality in patients undergoing noncardiac surgery have focused on elective surgery. The results from these studies may not be relevant to the present study since emergency surgery has been reported to correlate independently with development of life-threatening or fatal cardiac complications.[27] Moreover, approximately half of the patients presenting with a hip fracture are older than 80 yr, have a history of cardiovascular disease, and have ASA physical status III–V.[4] These elderly patients might therefore have an especially poor tolerance for the complications that are likely to occur during the stressful period of an emergency hospitalization.[28] Only one study,[7] however, prospectively investigated the incidence of cardiac death in patients with hip fractures who had CAD. Two patients (5%) who suffered from cardiac failure and myocardial infarct died. Enrollment of patients in that study, however, started only upon induction of anesthesia, and therefore, data regarding the stressful preoperative period were missing. In our study, 13 (19%) patients had adverse cardiac outcomes during their in-hospital stay, four of whom died. It is expected that morbidity and mortality will increase because of the rapid aging of the surgical population and greater prevalence of more advanced CAD.[1,27-29]

The results of the analysis of postoperative morbidity outcomes must be interpreted cautiously. Although the data for the entire perioperative period show that the incidence of perioperative adverse cardiac events was significantly higher in the control group compared with the epidural group, we did not control for intraoperative (blood loss, volume of fluid administered), postoperative (supplement of oxygen, fluid management, mobilization), or anesthetic (technique, drugs, dose) factors. Therefore, we classified the postoperative complications as secondary outcomes.
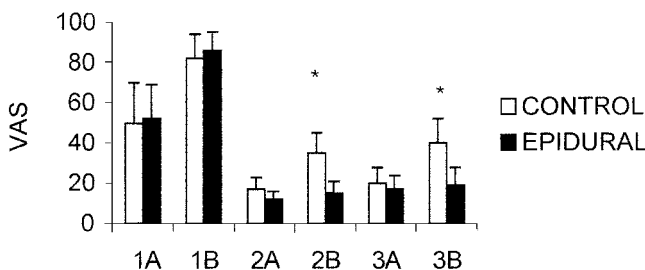

Fig. 2. Pain scores in the preoperative period. Pain scores were determined by a visual analog scale (VAS) graded from 0 (no pain) to 100 mm. Measurement times: 1 = before administration of analgesia; 2 = 1 h after administration of analgesia; 3 = before surgery. A = at rest; B = while the patient was slightly moving the fractured leg. *$P < 0.05$ between groups.

The mechanism by which early institution of epidural analgesia reduced preoperative cardiac events is unclear. Although there is little evidence that the stress response *per se* results in morbidity, several potentially detrimental physiologic effects are modulated through the stress response. Previous studies reported that stress may enhance perioperative hypercoagulable state and the release of cytokines and neuroendocrine hormones, which may dispose to vascular thrombosis and cardiac morbidity through reductions in myocardial oxygen supply or increases in demand.[18] The administration of epidural local anesthetic and opioids in the postoperative period to high-risk patients has been shown to suppress the stress response to surgery and to reduce the incidence of myocardial morbidity when compared with systemic opioids.[19,30,31] Hence, the observed effect of epidural analgesia on the incidence of cardiac outcome in the present study may in part be attributed to attenuation of the stress response.

Epidural administration of local anesthetics and/or opioids is an accepted technique to provide anesthesia and postoperative analgesia in patients undergoing lower extremity orthopedic surgery. Since these patients are at high risk for thromboembolic events, they frequently receive an anticoagulant postoperatively.[12] The decision to implement low-molecular-weight heparin thrombophylaxis in the presence of an indwelling catheter must be made with care since it may increase the risk of spinal hematoma.[32] For any low-molecular-weight heparin prophylaxis regimen, one of the most significant risk factors for the development of spinal hematoma is the timing of catheter removal. In our institution, therefore, the current guidelines are that the epidural catheter should be removed not less than12 h after the last dosing of enoxaparin.

Our study has several limitations. Most importantly, it was not conducted in a blinded fashion. Lack of blinding may have affected the reporting of the events. Routine screening, however, was performed with the use of cardiac isoenzyme levels and electrocardiography, which detected five of the seven preoperative cardiac complications. Moreover, the attending physicians were instructed to report to two other investigators (who were not aware of the patient's assignment) any change in the clinical status of the patients, and only then were management decisions made.

In the present study, heart rate and blood pressure were not monitored continuously, and therefore, we are not able to relate cardiac events to changes in hemodynamics. Nevertheless, prior studies revealed that the majority of perioperative cardiac events are not related to hemodynamic abnormalities.[3,21]

We chose only one dose of meperidine, and it may be speculated that a higher dose might have reduced the incidence of preoperative cardiac complications. However, higher doses of narcotics might have caused oxygen desaturation and respiratory depression, especially in this elderly population. Also, since traditional intramuscular injections of opioids provide inferior analgesia to patient-controlled analgesia with intravenous opioids, different results might have been achieved with the use of the latter technique to provide analgesia. As we have used this technique and dose for several years, we wished to compare this standard analgesic technique with the epidural regimen used in our institution. In the present study, when pain relief was inadequate, a supplement of analgesia was administered. Our results demonstrate that only two patients in the control group and three patients in the epidural group received supplemental analgesia.

Finally, concerns may arise as to the benefit of administering epidural analgesia in patients who have their operations within a few hours of admission. In the present study, the time from admission to surgery averaged 27 h. In most studies, patients waited on average 1.6–3.5 days between admission and surgery.[2,12,25,33] Results of studies of the optimal timing of surgery are contradictory. While few studies reported an increased mortality if patients had surgery within 24 h, others have demonstrated a clear advantage in operating early.[2,28] Nevertheless, the current prevailing recommendation is that ample time be taken to study and prepare patients with comorbidities. For these patients, epidural analgesia may prove to be most helpful.

The present study is important in being the first to show that the overall incidence of preoperative adverse cardiac events was higher in standard care group patients and that it can be reduced with early administration of an epidural analgesia. It was due to this fact that it was necessary to terminate the study. Despite the statistical significance of these findings, we believe that care should be taken in interpreting the difference in morbidity and mortality between the two groups. This is particularly important because the number of the observed events were few and the study groups were relatively small.

In conclusion, we found that early administration of epidural analgesia reduces the preoperative incidence of adverse cardiac outcomes in high-risk patients with fractured hips. This salutary effect of epidural analgesia indicates further study in large-scale trials that assess long-term outcome and the relationship between epidural analgesia, stress response to hip fracture, and adverse cardiac events.

References

1. Kannus P, Niemi S, Parkkari J, Palvanen M, Vuori I, Jarvinen M: Hip fractures in Finland between 1970 and 1997 and predictions for the future. Lancet 1999; 353:802–5

2. Lyons AR: Clinical outcome and treatment of hip fractures. Am J Med 1997; 103:51S–64S

3. Mangano DT: Perioperative cardiac morbidity. ANESTHESIOLOGY 1990; 72: 153–84

4. O'Hara D, Duff A, Berlin JA, Poses RM, Lawrence VA, Huber EC, Noveck H, Strom B, Carson JL: The effect of anesthetic technique on postoperative outcomes on hip fracture repair. ANESTHESIOLOGY 2000; 92:947–57

5. Marsch SCU, Schaefer HG, Skarvan K, Castelli I, Scheidegger D: Perioperative myocardial ischemia in patients undergoing elective hip arthroplasty during lumbar regional anesthesia. ANESTHESIOLOGY 1992; 76:518–27

6. Scheinin H, Virtanen T, Kentala E, Uotila P, Laitio T, Hartiala J, Heikkila H, Sariola-Heinonen K, Pullisaar O, Yli-Mayry S, Jalonen J: Epidural infusion of bupivacaine and fentanyl reduces perioperative myocardial ischaemia in elderly patients with hip fracture: A randomized controlled trial. Acta Anesthesiol Scand 2000; 44:1061–70

7. Juelsgaard P, Sand NPR, Felsby S, Dalsgaard J, Jakobsen KB, Brink O, Carsson PS, Thygesent K: Perioperative myocardial ischaemia in patients undergoing surgery for fractured hip randomized to incremental spinal, single-dose spinal or general anaesthesia. European J Anaesthesiology 1998; 15:656–63

8. Myers AH, Robinson EG, Van Natta ML, Michelson JD, Collins K, Baker SP: Hip fracture among the elderly: factors associated with in-hospital mortality. Am J Epidemiol 1991; 134:1128–37

9. Perez JV, Warwick CP, Case CP, Bannister GC: Death after proximal femoral fracture: An autopsy study. Injury 1995; 26:237–40

10. Riske EB: Factors influencing the primary mortality in the treatment of hip fracture. Injury 1970; 2:107–15

11. Beals RK: Survival following hip fracture: long term follow-up of 607 patients. J Chronic Dis 1972; 25:235–44

12. Morrison RS, Chassin MR, Siu AL: The medical consultant's role in caring for patients with hip fracture. Ann Int Med 1998; 128:1010–20

13. Mangano DT, Layug EL, Wallace A, Tateo I, for the Multicenter Study of Perioperative Ischemia Research Group: Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. N Engl J Med 1996; 335: 1713–20

14. Wallace A, Layug B, Tateo I, Li J, Hollenberg M, Browner W, Miller D, Mangano DT, for the McSPI Research Group: Prophylactic atenolol reduces postoperative myocardial ischemia. ANESTHESIOLOGY 1998; 88:7–17

15. Urban MK, Markowitz SM, Gordon MA, Urquhart BL, Kligfield P: Postoperative prophylactic administration of β-adrenergic blockers in patients at risk for myocardial ischemia. Anesth Analg 2000; 90:1257–61

16. McSPI-EUROPE Research Group: Perioperative sympatholysis: Beneficial effects of the α2-adrenoceptor agonist mivazerol on hemodynamic stability and myocardial ischemia. ANESTHESIOLOGY 1997; 86:346–63

17. Stuhmeier KD, Mainzer B, Cierpka J, Sandmann W, Tarnow J: Small oral dose of clonidine reduces the incidence of intraoperative myocardial ischemia in patients having vascular surgery. ANESTHESIOLOGY 1996; 85:706–12

18. Liu S, Carpenter RL, Neal JM: Epidural anesthesia and analgesia: Their role in postoperative outcome. ANESTHESIOLOGY 1995; 82:1474–506

19. Yeager MP, Glass D, Neff RK, Brinck-Johnsen T: Epidural analgesia and analgesia in high-risk surgical patients. ANESTHESIOLOGY 1987; 66:729–36

20. Mangano DT, Hollenberg M, Fegert G, Lou Meyer M, London MJ, Tubau JF, Krupski WC: Perioperative myocardial ischemia in patients undergoing noncardiac surgery: I. Incidence and severity during the 4 day perioperative period. The Study of Perioperative Ischemia (SPI) Research Group. J Am Coll Cardiol 1991; 17:843–50

21. Fleming TR, Harrington DP, O'Brien PC: Designs for group sequential test. Control Clin Trials 1984; 5:348–61

22. Tition Y, Eshkol Z, Horesh T, Suderi M: Perioperative mortality after neck of femur surgery in the elderly. Harefuah 2000; 139:18–22

23. Boereboom F, Raymakers J, Duursma S: Mortality and causes of death after hip fracture in the Netherlands. Neth J Med 1992; 41:4–10

24. Bergqvist D, Fredin H: Pulmonary embolism and mortality in patients with fractured hips: A prospective consecutive series. Eur J Surg 1991; 157:571–4

25. Sutcliffe AJ, Parker M: Mortality after spinal and general anaesthesia for surgical fixation of hip fracture. Anaesthesia 1994; 49:237–40

26. Nettleman M, Alsip J, Schrader M, Schulte M: Predictors of mortality after acute hip fracture. J Gen Int Med 1996; 11:765–7

27. Goldman L, Caldera DL Southwick FS, Nussbaum SR, Murroy B, O'Malley TA, Goroll AH, Caplan CH, Nolan J, Burke DS, Krogstad D, Carabello B, Slater EE: Cardiac risk factors and complications in noncardiac surgery. Medicine 1978; 57:357–70

28. Ellison N, Mull TD: Unique anesthetic problems in the elderly patient coming to surgery for fracture of the hip. Orthopedic Clin North Am 1974; 5:493–508

29. Lu-Yao GL, Baron JA, Barret JA, Fisher ES: Treatment and survival among elderly Americans with hip fractures: A population based study. Am J Public Health 1994; 84:1287–91

30. Beattie WS, Buckley DN, Forrest JB: Epidural morphine reduces the risk of postoperative myocardial ischaemia in patients with cardiac risk factors. Can J Anaesth 1993; 40:532–41

31. Tuman KJ, McCarthy RJ, March RJ, DeLaria GA, Patel RV, Ivankovitch AD: Effect of epidural anesthesia and analgesia on coagulation and outcome after major vascular surgery. Anesth Analg 1991; 73:696–704

32. Horlocker TT: Low molecular weight heparin and neuroaxial anesthesia. Thromb Res 2001; 101:V141–54

33. Sorenson RM, Pace NL: Anesthetic techniques during surgical repair of femoral neck fractures: A meta-analysis. ANESTHESIOLOGY 1992; 77:1095–104