Hypotensive epidural anesthesia for total hip arthroplasty

A review

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Hypotensive epidural anesthesia provides arterial hypotension to maintain a mean arterial pressure of 50 mmHg and it can be used to reduce blood loss during total hip replacement. The technique combines an extensive epidural blockade with an intravenous infusion of low-dose epinephrine. This results in arterial hypotension, but with preservation of central venous pressure, heart rate, stroke volume, cardiac output, and an augmentation of blood flow to the lower extremity. The technique does not appear to adversely affect cardiac, renal, or cerebral function and is used safely in patients with hypertension, ischemic heart disease, and in the elderly.

Intraoperative blood losses during primary total hip replacement are between 100 and 300 mL. Perioperative transfusions have declined with the introduction of the technique. Radiological evidence of improved fixation of cemented acetabular components has been observed. Rates of deep-vein thrombosis are low: 2–3% proximal deep-vein thrombosis with an overall rate of 10%. In-hospital mortality is 0.1%; lower than previously published rates. In conclusion, hypotensive epidural anesthesia is safe and provides a number of advantages over conventional anesthetic techniques for total hip replacement.

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Submitted 95-09-07. Accepted 95-10-05

A technique for providing hypotensive epidural anesthesia (HEA) during total hip replacement (THR) has been used in over 8,000 cases at the Hospital for Special Surgery in New York City during the past 8 years. We will describe the technique, physiology, and clinical applications as well as its beneficial effects on postoperative venous thromboembolism.

Historical background

Extensive spinal anesthesia was used in the USA in the 1920s (Koster 1928) and in Britain in the 1940s (Griffiths and Gillies 1948) for surgery of the abdomen and thorax. Although it provided a dry surgical field, the technique was abandoned because of circulatory and respiratory difficulties. Later, a dry surgical field using hypotensive anesthesia has been provided by vasodilators or cardiac depressants under general anesthesia (GA) (Miller 1990). The purpose of developing hypotensive epidural anesthesia (HEA) for THR was to combine the virtues of reduced intraoperative blood loss from induced hypotension with the lower risk of postoperative deep-vein thrombosis and thromboembolism associated with epidural anesthesia (Modig 1988a, 1988b, Sharrock et al. 1990b).

Development of the technique

The first approach was to provide an extensive epidural block to T4 or above and allow the blood pressure to decrease spontaneously. As soon as mean arterial pressure (MAP) reached 50 mmHg, intravenous fluid was rapidly infused to maintain this pressure. Unfortunately, although MAP could be reduced with this approach, both heart rate and central venous pressure (CVP) declined and cardiac output fell 30–50% (Sharrock et al. 1990b). Some patients even became nauseated or yawned in association with the low cardiac outputs (≤1.8 L/min/m^2) and bradycardia (less than 50 bpm). Several vasopressors were used to augment cardiac output, including dopamine, dobutamine, isoproterenol, ephedrine and epinephrine. It was found that epinephrine in low doses (1–5 µg/min) stabilized heart rate, CVP and cardiac output during hypotension. Patients could be kept awake if necessary, they were lucid, and asymptomatic. This technique thus provided hemodynamic stability with a dry surgical field and preserved brain function. Subsequent studies have demonstrated that patients have a reduced intraoperative blood loss, fewer perioperative blood transfusions (Sharrock 1993a), a lower rate of deep vein thrombosis (Sharrock et al.

1993b, Lieberman et al. 1994), and a low perioperative mortality rate (Sharrock et al. 1995a).

Technique

The following equipment is used routinely: an arterial line, an anesthetic monitor capable of displaying arterial and central venous pressures, an electrocardiogram, pulse oximeter, and one or two infusion pumps. The epidural injection is performed ideally at the L1–2 interspace by injecting 15–25 mL of a potent local anesthetic (2% lidocaine with epinephrine or 0.75% bupivacaine plain), depending on age and body mass. This large dose of a concentrated local anesthetic is used to ensure a deep blockade up to T4-T1, providing both excellent surgical anesthesia and an extensive sympathetic blockade. A catheter is placed in the event that additional anesthetic may be needed intraoperatively and to provide the option of a postoperative patient with controlled epidural analgesia.

Immediately after the epidural local anesthetic is injected, an intravenous infusion of epinephrine is started, via either a central venous or a peripheral intravenous catheter. The epinephrine infusion we use contains 1 mg of epinephrine in 250 mL of saline (4 µg/mL). The initial infusion rate is usually 2 µg/min (30 mL/hr), but is adjusted during the next 10–20 min to achieve an MAP of about 50 mmHg. Usually this degree of hypotension is obtained within 10–15 min.

If the MAP does not fall rapidly enough, the rate of administration of epinephrine can be reduced. Conversely, if the MAP falls rapidly, the dose of epinephrine is increased and intravenous fluid (300–500 mL) infused. Thus, adjustments in the epinephrine rate and intravenous fluid are made to maintain a MAP of 50 mmHg.

It is usually not necessary to infuse excessive amounts of intravenous fluid. However, if the heart rate increases and/or the blood pressure declines too rapidly, the patient is probably hypovolemic. In this situation, the epinephrine dose should be increased to 4–7 µg/min to maintain a MAP of 50 mmHg and 300–500 mL of lactated Ringer's solution rapidly infused. As the fluid is infused, the amount of epinephrine required usually decreases. When the MAP is stable at 50 mmHg with a dose of epinephrine of less than 5 µg/min, the rate of administration of fluids can be slowed. Most patients undergoing primary THR require no more than 1,000-1,500 mL of lactated Ringer's solution during surgery using hypotensive epidural anesthesia (intraoperative blood loss is usually between 100 and 300 mL) (Sharrock et al. 1992, 1993a, 1993b, 1994a, Lieberman et al. 1994). Central venous pressure monitoring facilitates precise fluid administration.

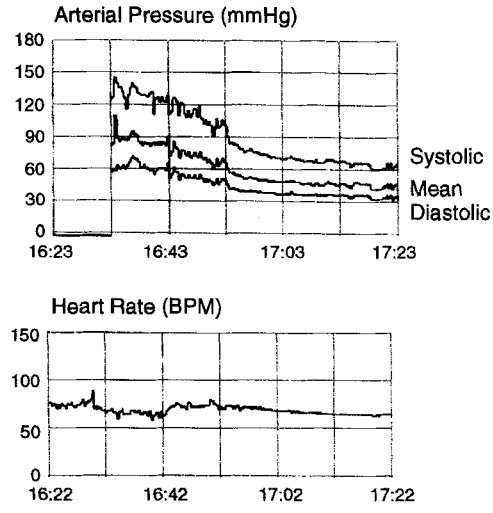


Figure 1. Epidural injection of 20 mL 0.75% bupivacaine at L1-2 is performed at 16:42 and an infusion of low-dose epinephrine 2 µg/min started. Note the variation in heart rate prior to and immediately after the epidural injection. However, by 17:00, there is no variability in heart rate consistent with the abolition of cardiac sympathetic nerve function by the extensive epidural blockade.

Hypotensive epidural anesthesia is best performed with an upper thoracic level (T4 or above) for several reasons. First, the high level provides analgesia to the lateral chest wall, making it more comfortable for patients to lie on their sides for an extended period of time. Secondly, the extensive blockade produces a deep sympathetic blockade providing effective vasodilation as well as blockade of the cardiac accelerator fibers. This not only facilitates the hypotension (from the extensive vasodilation) but prevents reflex tachycardia, since the cardiac sympathetics are blocked. Beat-to-beat variability is also suppressed (Figure 1). The dose of intravenous epinephrine can then be adjusted to achieve the appropriate heart rate, blood pressure, filling pressures, and a stable cardiac output. This is somewhat analogous to modern general anesthesia, wherein one intubates and paralyzes the patient, and adjusts the ventilator to the desired end-tidal carbon dioxide level. With the extensive epidural anesthesia, one "paralyzes" the circulation and adjusts the epinephrine infusion rate according to the desired blood pressure and heart rate.

The technique is best performed when the heart rate is between 55 and 80 bpm. Rates over 80 bpm may reflect volume depletion and should be corrected

with intravenous fluid. In addition, tachycardia may induce ischemia in patients with coronary artery disease during hypotension. Heart rates of less than 55 bpm lead to a lower cardiac output and may portend severe bradycardia/asystole (Tarkkila and Kaukinen 1991, Carpenter et al. 1992, Jacobson et al. 1992) so the rate should be increased by increasing the dose of epinephrine or adding intravenous isoproterenol.

An alternative method of inducing hypotension with epidural anesthesia is to establish a T6–10 level and lower the arterial pressure with a vasodilator, such as sodium nitroprusside (SNP). There are a number of problems with this technique. First, the patients tend to be uncomfortable lying on their side, unless an upper thoracic level is achieved. Secondly, reflex tachycardia may develop with the induction of hypotension, as the cardiac sympathetic nerves are not blocked. Finally, SNP is a venodilator which lowers CVP and may predispose patients to acute bradycardia or asystole (Kennedy et al. 1968, Tarkkila and Kaukinen 1991, Carpenter et al. 1992, Jacobson et al. 1992). For these reasons, this technique is not advocated. However, if a vasodilator is required, SNP has the advantage of a short duration of action. Very low doses of SNP must be used (1 µg/min) concurrently with an epinephrine infusion of 1–2 µg/min. The SNP infusion is slowly increased until the MAP declines. Alternatively, longer acting intravenous vasodilators, such as droperidol 1.25–2 mg or Apresoline 5–10 mg, may be used. A third way to lower blood pressure is to inject additional local anesthetic via the epidural catheter.

Extensive sympathetic blockade can also be obtained with a high dose of spinal anesthesia (20 mg bupivacaine) or using combined spinal epidural anesthesia (CSE). Following the initial dose of intrathecal bupivacaine (15–20 mg), the epinephrine infusion is begun at 2 µg/min and adjusted, as required, to achieve an MAP of 50 mmHg. If the anesthesia level is insufficient to reduce MAP to 50–60 mmHg, additional local anesthetic can be administered via the epidural catheter.

If the epidural blockade does not extend above T5, the blood pressure may not decline sufficiently. This occurs in several situations. First, the dose of local anesthetic may be insufficient. Secondly, the interspace may be too low: T12–L1 or L1–2 interspaces are ideal as proximal spread occurs more reliably following injection at upper rather than lower lumbar interspaces (Sharrock et al. 1984). Finally, in patients less than 60 years of age, epidural spread of local anesthetic is less extensive (Sharrock 1978). Therefore, in younger patients, it is all the more important to perform the epidural block at an upper lumbar interspace (T12–L1 or L1–2) and inject 20–25 mL local anesthetic initially, and to be prepared to use additional local anesthetic via the catheter, if the MAP does not decline adequately.

The blood pressure may not fall if the central venous pressure is too high, particularly if too much intravenous fluid has been given. For this reason, fluids are usually restricted during the epidural injection and they are given rapidly only if the heart rate increases or the pressure declines too fast. This method must not be used in severely volume-depleted patients (e.g., in trauma patients), as acute severe hypotension can occur, leading to cardiac standstill (Kennedy et al. 1968). Patients should have a normal blood volume prior to starting the anesthetic. The central venous pressure can be assessed by examining the neck veins or by using a central venous pressure cannula.

It is important to induce and maintain an extensive sympathetic blockade. Our experience suggests that epidural blockade during surgery begins to recede approximately 1–1 1/2 hrs after the administration of 0.75% bupivacaine plain (Sharrock 1993b). For this reason, 5–10 mL of local anesthetic is usually reinjected via the epidural catheter every 60 min, if the surgical procedure is to last for more than 2 hours. As the epidural blockade recedes, vasoconstriction occurs. In this situation, the arterial pressure may remain low if additional blood loss occurs, resulting in a decreased cardiac output which may predispose to deep vein thrombosis and tissue acidosis.

Figures 2–5 show trends of heart rate and arterial pressure, with or without central venous or pulmonary artery pressure. They demonstrate the stability of the heart rate, stable low blood pressure and adjustment of fluid and epinephrine to maintain hemodynamic stability.

Patients with altered responses

Patients with hypertension, ischemic heart disease or glaucoma who are receiving beta-blockade therapy have an altered response to epidural anesthesia (Reiz 1986), and may develop a reduction in heart rate, cardiac output, and stroke volume during HEA. If an intravenous infusion of epinephrine is given, blood pressure increases without any increase in heart rate or cardiac output ("unopposed alpha effect"). The net effect is either bradycardia or no hypotension. An intravenous infusion of isoproterenol (0.5–2 µg/min) maintains heart rate but, when used alone, it often results in hypotension (McLean et al. 1967), a reduction in CVP, and a variable effect on cardiac output.

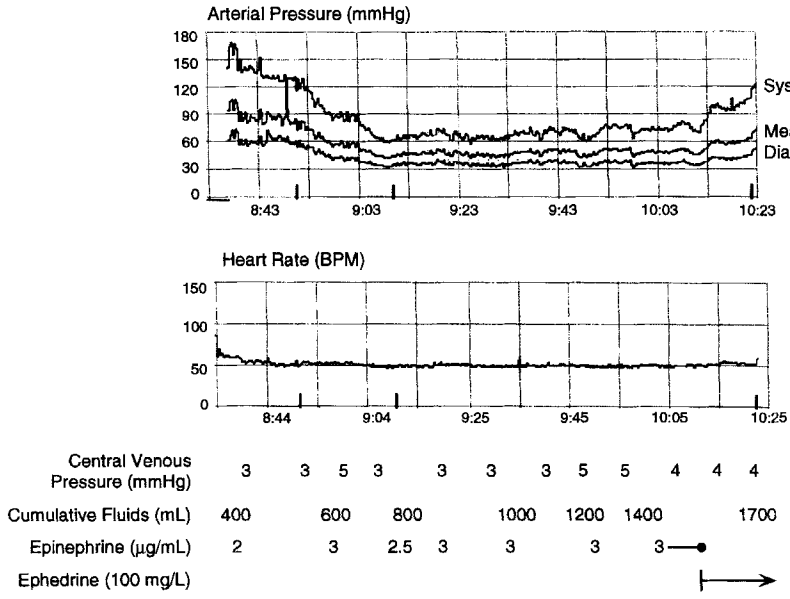
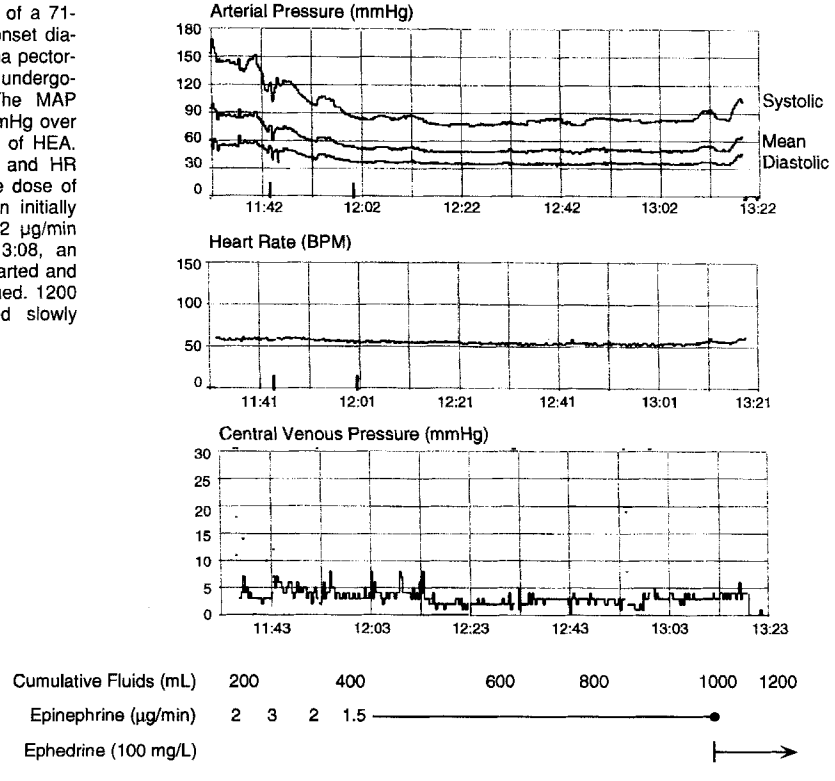


Figure 2. Trend recording of heart rate and arterial pressure during THR performed with HEA. Note the decline of MAP from 105 to 50 mmHg throughout surgery. Heart rate declined from 60 to 50 bpm with induction of HEA. Central venous pressure was stable at 3–5 mmHg throughout. Epidural injection was performed at 8:50. MAP declined from 90 to 50 mmHg in 15 min. The epinephrine dose was 2 µg/min initially, it was increased to 3 µg/min as the MAP fell but reduced to 2 µg/min at 9:05 as MAP was stabilized with a further 200 mL crystalloid. Thereafter, 500 mL fluid was infused over the next 30 min and the epinephrine dose was increased to 3 µg/min to maintain MAP at 50 mmHg. The acute decline in MAP at 9:58 and 10:09 correlates with relocating the hip joint. Ephedrine infusion 100 mg/L was begun at 10:11 and the dose of epinephrine discontinued. MAP increased to 70 mmHg at the end of surgery.

Figure 3. Trend recording of a 71-year-old male with adult-onset diabetes, hypertension, angina pectoris, and chronic bronchitis undergoing THR under HEA. The MAP declined from 90 to 50 mmHg over 20 min with the induction of HEA. Central venous pressure and HR remained unchanged. The dose of epinephrine was 2 µg/min initially and ranged from 1.5 to 2 µg/min throughout surgery. At 13:08, an ephedrine infusion was started and the epinephrine discontinued. 1200 mL of fluid was infused slowly throughout surgery.



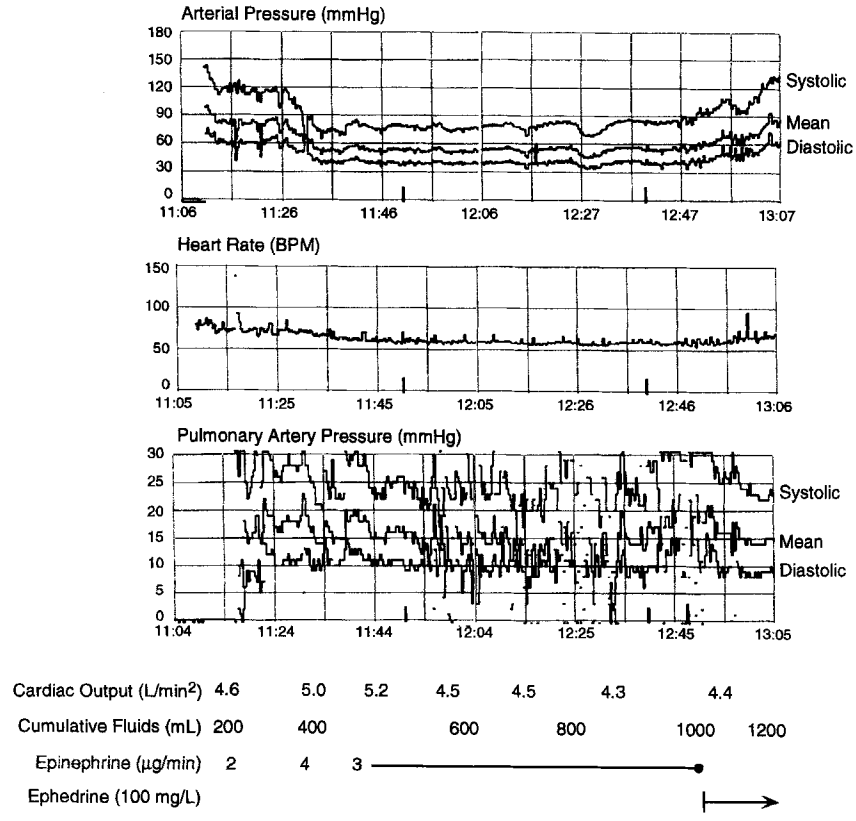


Figure 4. Trend recordings of heart rate, arterial, and pulmonary artery pressures during HEA for a primary THR in a 70-year-old man who has had a coronary artery bypass graft and bilateral carotid artery disease. Note that MAP was 100 mmHg prior to the anesthesia; it declined to 90 mmHg with sedation during insertion of the pulmonary artery catheter. At 11:26 the epidural anesthesia was administered and over the next 10 min the MAP declined to 50 mmHg and remained at 50–55 mmHg throughout surgery. Heart rate declined from 70 to 60 bpm with the onset of HEA. Pulmonary artery pressure and cardiac output remained unchanged.

An infusion of epinephrine (2 µg/min) was started prior to administering the epidural anesthesia (11:20) and was increased to 4 µg/min as the MAP declined. 400 mL of fluid was infused with the onset of the epidural and the epinephrine infusion decreased to 3 µg/min. At 11:46, the epinephrine infusion was reduced to 1 µg/min after an infusion of ephedrine (100 mg/L). The total fluid during the procedure was 1200 mL.

However, using a combination of epinephrine and isoproterenol infusions, a stable MAP of 50 mmHg with a satisfactory heart rate can usually be achieved in patients on beta-blockade therapy (Figure 5). The infusion rates of these drugs required to achieve hypotension with a heart rate of at least 55 bpm vary between individuals, probably reflecting various degrees of beta-blockade and idiosyncratic responses.

Patients with hypertension, heart failure, or ischemic heart diseases who are taking angiotensin converting enzyme (ACE) inhibitors behave like patients who are volume-depleted and tend to require higher doses of epinephrine to maintain blood pressure. Under normal circumstances, epinephrine releases renin, which acts via ACE to produce the potent vasoconstrictor, angiotensin (Thames 1984). In patients taking ACE inhibitors, the renin released by epinephrine does not produce angiotensin (Packer 1992a, b), so that the vasoconstrictor action of epinephrine is obtunded. Many of these patients require intravenous infusion of both phenylephrine and epinephrine to maintain blood pressure without tachycardia. Alternatively, additional intravenous fluid can be given to keep the epinephrine infusion rate less than 5 µg/min.

Physiology

Circulation

The circulatory effects of HEA are due to both the extensive sympathetic block from the epidural anesthetic and the low-dose intravenous epinephrine infusion. The sympathetic block from the epidural anes-

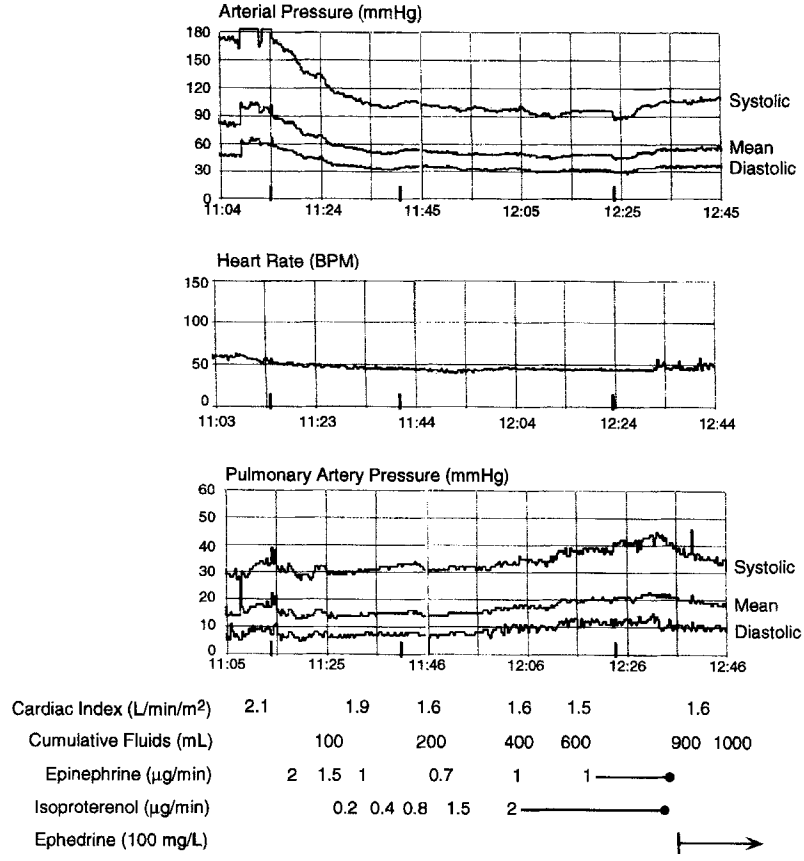


Figure 5. An 86-year-old female undergoing primary THR under HEA. Past history includes aortic valve replacement, left ventricular hypertrophy, hypertension, heart failure, and glaucoma. Medications include Lanoxin, diltiazem, Bumex, Pepcid, and Timoptic eye drops.

MAP declined from 100 to 50 mmHg 20 min following the epidural injection and HR fell from 60 to 45 bpm. Epinephrine was initially infused at 2 µg/min but was reduced to 1.0 µg/min and isoproterenol given, initially at 0.2 µg/min but it was increased to 2.0 µg/min during surgery. HR remained at 45 bpm throughout surgery. Cardiac index was 2.1 initially and ranged from 1.5 to 1.6 during surgery. Pulmonary artery pressure remained stable. Following insertion of a cemented femoral component, the hip was reduced at 12:23. Note the increase in PAP and reduction in arterial pressure at this point. Arterial pressure was increased using ephedrine at the end of surgery. Note the decline in PAP at 12:45 with ephedrine suggesting clearance or adaptation to the embolic material within the lung.

thesia dilates the arterioles and veins and suppresses both the inotropic and chronotropic activity of the heart (Stanton-Hicks 1975, Stanton-Hicks et al. 1987). If untreated, this leads to acute hypotension, bradycardia, and a significant reduction in cardiac output (Stanton-Hicks 1975, Sharrock et al. 1990b). Epinephrine modifies the response by preserving preload (CVP) and stimulating the adrenergic receptors in the heart to maintain heart rate and stroke volume (Sharrock et al. 1990b, 1992, Zayas et al. 1993, Bading et al. 1994). The net effect is a decline in MAP to 50 mmHg, with no change in heart rate, central venous pressure, or cardiac output. If other vasopressors, such as norepinephrine or phenylephrine, are used, MAP will decline, but also heart rate, central venous pressure and cardiac output (Sharrock et al. 1993c, Zayas et al. 1993, Bading et al. 1994). Epinephrine is the only vasopressor we have used that can result in a normal cardiac output with hypotension. Beta agonists, such as isoproterenol (McLean et al. 1967) or dobutamine (Takasaki 1988), lead to a decline in filling pressure and an increase in heart rate. In many cases this is associated with a decline in cardiac output and the MAP can be difficult to stabilize.

Respiration

Breathing is seldom impaired, because the epidural dose -response characteristics are such that, with a lumbar injection, it is difficult to achieve upper cervi-

cal anesthesia. With a T1–4 sensory block, the intercostal muscles and abdominal muscles are paralyzed and patients have difficulty in coughing (Sharrock 1993b). In spite of this, they can breath well, as diaphragm function is preserved. Sedated patients breathing spontaneously with nasal oxygen, 3 L/min, demonstrate slight hypercardia p_aCO_2 43–48 mmHg with normoxia p_aO_2 150–250 mmHg (Sharrock et al. 1990b, Bading et al. 1993). Patients with chronic obstructive lung disease tolerate extensive thoracic epidural blockade (Groeben et al. 1995).

Brain

No cerebral blood flow measurements have been performed with this technique. Though most patients elect to be sedated, they can be kept awake throughout surgery, remain lucid, and feel normal, in spite of a MAP of 50 mmHg. Currently, we are performing a battery of preoperative and postoperative cognitive function tests on 240 elderly patients. So far, we have not noted any cognitive disturbances, compared to patients who have had normotensive anesthesia. Postoperative stroke occurs in less than 1 in 1,000 cases (Sharrock et al. 1991b). We plan to measure the velocity of blood flow in the middle cerebral artery in patients undergoing HEA.

Kidneys

With induction of HEA, there is a marked decline in perfusion pressure at the glomerulus, resulting in a decline in filtration pressure. When epinephrine is used to support the circulation at a MAP of 50 mmHg, glomerular filtration and renal blood flow decline by approximately 50%. Sodium excretion and urine volume decline even more (Zayas et al. 1993). In spite of this, clinical evidence of renal dysfunction is uncommon following HEA for THR. In a series of 194 patients who had serum creatine measured pre- and postoperatively, no patient had an increase in creatinine of more than 0.3 mg/dL (unpublished observations). In a prospective study of 987 THRs, no patient developed postoperative renal failure (Sharrock et al. 1991b).

Hormonal effects

With extensive epidural blockade in elderly patients, there is an almost complete sympathectomy. Blood levels of both epinephrine and norepinephrine decline (unless epinephrine is infused intravenously) (Zayas et al. 1993). Plasma renin activity increases slightly when epinephrine is infused but decreases (in spite of the hypotension) when phenylephrine is used to maintain MAP at 50–60 mmHg (Zayas et al. 1993). No changes in insulin, growth hormone, cortisol, or enteric hormonal levels have been measured.

Distribution of blood flow

Epidural blockade is known to increase blood flow to the skin of the feet, but not to augment skeletal muscle blood flow (Wright and Cousins 1972). By contrast, low-dose epinephrine increases blood flow to skeletal muscle and adipose tissue (Freyschuss et al. 1986). In 12 elderly patients about to undergo THR, calf blood flow increased 67% following induction of HEA (MAP of 48 mmHg), using low-dose intravenous epinephrine infusion. By contrast, there was a 30% decline in calf blood flow if norepinephrine (but no epinephrine) was used (Bading et al. 1994). This demonstrates that, with HEA using epinephrine, blood flow is redistributed to the muscles of the legs. This would be expected to reduce deep venous stasis intraoperatively as well as in the immediate postoperative period (Thomas 1985). The vasodilation from the low-dose epinephrine may also contribute to arterial hypotension (Stanton-Hicks et al. 1973).

Local anesthetic levels

Arterial plasma concentrations of bupivacaine have been measured in 49 patients using 30 mL 0.75% bupivacaine (Sharrock et al. 1995c). The mean plasma level was 2–3 µg/mL—the toxic threshold level is said to be 4 µg/mL (Sharrock et al. 1991a, 1995c). In spite of using large doses of local anesthetic, we have never seen a toxic reaction to bupivacaine, unless the local anesthetic was injected intravenously.

Anesthetic technique for revision THR or one-stage bilateral THR

To maintain epidural anesthesia and hypotension for prolonged revision THR, several modifications are required. Adequate sedation with intermittent intravenous doses of midazolam or an infusion of Pentothal (150–300 mg/hr) helps keep the patient comfortable. Epidural or intravenous fentanyl, central venous Valium or nasal nitrous oxide is also useful as an adjunctive sedative agent. The choice of sedative agent is not so important; rather the aim is to keep the patient comfortable, breathing spontaneously and preferably amnesic.

With revision surgery, the epidural is usually "topped off" with 5–7 mL 0.75% bupivacaine every hour to maintain the intense neural blockade with

complete sympathectomy. We observed no disadvantage from a prolonged period of hypotension.

It is important to position patients carefully. They must be comfortable, lying on their side. Heavy patients may be troubled by dependent shoulder pain. This is best handled with a high thoracic sensory level so that the axillary roll, which takes much pressure off the shoulder, does not cause discomfort in the chest wall. With hypotension, excessive pressure can compress blood vessels, leading to ischemia, especially if an anterior post is used to stabilize the pelvis. This can lead to obstruction of the femoral vein and possibly of the femoral artery. If protracted for several hours, it can produce a clinical picture similar to a compartment syndrome in the dependent leg. This may lead to a nerve injury and rhabdomyolysis of the thigh (Smith et al. 1989).

Hypotensive epidural anesthesia in high-risk cases

The average age of patients undergoing primary THR at Hospital for Special Surgery is 63 years. One third have hypertension, 14% have known ischemic heart disease, 8% have diabetes, and 1% have had strokes (Sharrock et al. 1991b). Nowadays, more patients who tend to be older are returning for revision arthroplasty, so it is important to define the role of HEA in these high-risk cases.

Hypertension

In a prospective study of 987 THRs, 36% had hypertension (Sharrock et al. 1991b). Patients with hypertension had their MAP reduced to a similar extent as normotensive patients without a difference in postoperative morbidity or mortality. Hemodynamic measurements were performed in patients with and without hypertension. Patients with hypertension (with or without left ventricular hypertrophy) had a preserved heart rate, filling pressures, and cardiac output during HEA with an MAP of 50 mmHg. A similar hemodynamic response was noted in normotensive patients. This study demonstrated that patients with treated hypertension respond well to HEA. Brain and kidney function were well preserved, in spite of concerns about altered autoregulation in these organs in the presence of essential hypertension (Strandgaard 1976).

Ischemic heart disease

In this study (Sharrock et al. 1991b), 143 of the 987 patients had ischemic heart disease, defined by a prior myocardial infarction, angina pectoris, or a prior coronary artery bypass graft or angioplasty. These patients had their MAP reduced to a similar extent during surgery as the patients without ischemic heart disease. The preoperative mean systolic pressures were 154 mmHg in patients with arteriosclerotic heart disease (ASHD) and 146 mmHg in those without ASHD. The average lowest recorded systolic pressures were 73 mmHg in patients with ASHD (a 54% decline) and 69 mmHg in patients without ASHD (53% decline). Postoperatively, one of these patients with ischemic heart disease died of a myocardial infarct. The degree of hypotension used in patients with ASHD varies among anesthesiologists at our institution. Mean arterial pressures during surgery range from 50 to 70 mmHg. The degree of hypotension, however, does not appear to affect outcome and this issue is currently being studied.

We do not believe the technique is any safer in patients with ischemic heart disease, but it does not appear to increase the rate of cardiac complications. HEA does not induce myocardial ischemia probably because, as the blood pressure falls, so also does the metabolic requirement of the heart (Lynn et al. 1952, Hackel et al. 1956, Braunwald 1971). In addition, blockade of the cardiac sympathetic nerves may modulate coronary artery tone (Blomberg et al. 1990) minimizing the risk of myocardial ischemia (Braunwald 1971).

Congestive heart failure

The circulatory response to HEA is normal in patients with impaired ventricular function (Sharrock et al. 1994b). Cardiac output and stroke volume were measured following the induction of HEA in a group of patients with poor cardiac function. Patients with a history of congestive heart failure and those with low preoperative cardiac output (<2.5 L/min/m^2) had an increase in stroke volume and cardiac output following induction of the HEA. This is not surprising, as many of these patients have elevated basal levels of renin and noradrenaline, and treatment with vasodilators and ACE inhibitors improves cardiac performance and life expectancy (Packer 1992b).

Elderly patients

This technique has been used in many elderly patients. Close to 10% of our patients undergoing THR are over 80 years of age. To assess further the effects of HEA in elderly patients (>70 years of age), we are currently performing a randomized trial of maintaining patients during THR surgery with a MAP of either 45–55 mmHg or 60–70 mmHg and assessing cognitive and cardiac effects at 1 week and 3 months following surgery.

Patients with diseases of the spine

Epidural or spinal anesthesia can be technically difficult to perform in patients with spinal deformities. In patients who have had prior decompressive laminectomies, spine fusion, or disc excision, the epidural space can usually be entered at several interspaces above the site of prior surgery (Sharrock et al. 1990c). Severe spinal stenosis is not a contraindication for HEA. Epidural entry in patients with ankylosing spondylitis is technically challenging. However, in our experience, successful lumbar epidural anesthesia can be achieved in about half of these patients (Sharrock et al. 1990c). Alternatively, the caudal approach can be used or general anesthesia after securing an airway with a bronchoscope.

Mortality

In the USA, the in-hospital mortality rate in 1979 was 1% for patients undergoing THR who were covered by medicare insurance (usually people over 65 years of age) but decreased to 0.7% by 1988 (Peterson et al. 1990). In a series of 1162 cases in the U.K. in 1990–91, the mortality rate was 0.9% within 30 days after surgery. Death from pulmonary embolism was 0.3% (Warwick et al. 1995). At the Hospital for Special Surgery, the in-hospital mortality rate from 1981 through 1985 was 0.4% (13 of 3622 patients died) (Sharrock et al. 1995a). From 1987 through 1991, after the introduction of HEA, the mortality rate was 0.1% (6 of 5869 patients died, p 0.03). Of note was that there were no deaths in 392 patients undergoing one-stage bilateral THR performed with HEA. Deaths from pulmonary embolism declined sixfold from 0.12% in 1981–85 to 0.02% in 1987–91 (p 0.03). When properly performed, HEA is not more dangerous than normotensive anesthesia. The question is: is it safer and, if so, in whom is it contraindicated?

Contraindications

Hypotensive epidural anesthesia is contraindicated in patients with severe aortic or mitral stenosis. In these patients, cardiac output is dependent upon a preserved or enhanced preload, so it is better not to induce hypotension with epidural anesthesia in such cases. Patients with severe hypertrophic subaortic stenosis typically show a decline in cardiac output with this technique. Cardiac output and stroke volume may be preserved in patients with moderate or mild aortic stenosis with HEA. Nevertheless, it is best to monitor these patients carefully with pulmonary artery catheters perioperatively.

A prior stroke is not a contraindication for HEA since most CVAs are embolic events. However, if patients have severe stenosis (>80% occlusion) of either the carotid or vertebral arteries, HEA should not be performed. In these patients, epidural anesthesia can be performed, to maintain systolic pressures at more than 100 mmHg.

In patients with renal failure but not on dialysis (Cr >2.5 mg/dL) or with renal allografts, MAP are kept in the 65–75 mmHg range with either a phenylephrine or dopamine infusion rather than with epinephrine. Phenylephrine preserves renal blood flow during HEA (Zayas et al. 1993).

Patients with first or second degree heart block may develop progression of heart block due to the combined effect of the cardiac sympathectomy and the local anesthetic on the conducting system. In these cases, it may be prudent to use spinal anesthesia (bupivacaine 15 mg) and keep the anesthetic level below T6. Isoproterenol infusion may preserve heart rate in patients with bradycardia. Patients with right or left bundle branch block respond normally to HEA.

Complications

The major intraoperative risks with HEA are high epidural or total spinal anesthesia (Bromage 1978) and severe bradycardia or asystole (Tarkkila and Kaukinen 1991, Carpenter et al. 1992, Jacobson et al. 1992). High epidural is defined as difficulty in breathing after epidural injection due to a sensory level extending to the upper cervical dermatomes. In our experience, it occurs in approximately 0.3% in three main situations: in elderly patients given larger doses of local anesthetic (>20 mL); in patients given additional doses of local anesthetic, administered via an epidural catheter; and in patients who have had prior lumbar spine surgery. These cases are managed by assisting or controlling ventilation for 45 or 60 min and supporting the circulation with the epinephrine infusion.

Severe bradycardia is a common problem, unless a beta-agonist such as epinephrine, is used (Sharrock et al. 1993c). Heart rates usually decline to less than 60 bpm if phenylephrine, norepinephrine or fluids are used as the sole support of the circulation. Acute bradycardia develops secondary to venodilatation, volume depletion, Valsalva maneuver or emotional reactions (Carpenter et al. 1992, Jacobson et al. 1992). If a beta-agonist is not administered, the

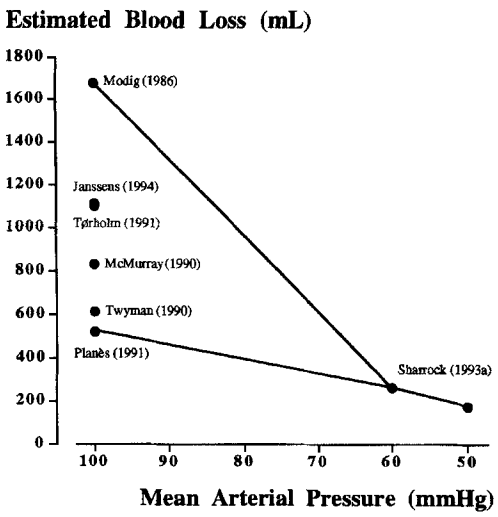


Figure 6. The relationship between mean intraoperative measured blood losses from published series and the intraoperative blood pressure during surgery. The blood losses at MAPs of 50 and 60 mmHg were with hypotensive epidural anesthesia whereas the estimated blood losses in the other studies were with normotensive anesthesia (assumed to be a MAP of 100 mmHg).

bradycardia may rapidly progress to asystole. Early treatment of severe bradycardia with epinephrine 8 µg or ephedrine 10–25 mg intravenously restores heart rate. Higher doses may be necessary for asystole. The best approach is to prevent bradycardia by maintaining heart rate above 60 bpm with an epinephrine infusion (or isoproterenol, if necessary).

What is the optimal blood pressure?

A MAP of 50 mmHg is widely considered to be the safe lower limit of hypotension, as it is the lower limit of autoregulation of the cerebral circulation (Miller 1990). Nevertheless, irreversible changes in cerebral function do not occur until perfusion pressure falls to 20–30 mmHg in animals (Fitch et al. 1976). However, it is appropriate to question what is the advantage of lowering MAP to 50 mmHg rather than perhaps 60 mmHg during surgery, unless it offers some advantage, particularly in older patients.

We addressed this question by randomly assigning 40 patients undergoing primary THR to an intraoperative MAP of either 50 ± 5 mmHg or 60 ± 5 mmHg (Sharrock et al. 1993a). Subjective assessment of bleeding by the surgeon (EAS) was found to be significantly greater at 60 ± 5 mmHg during exposure of the hip joint, reaming of the acetabulum and the femur. The mean estimated intraoperative blood loss was 179 (100–320) mL in the 50-mmHg group and 263 (130–500) mL in the 60-mmHg group. The durations of surgery were similar for both groups. This showed that a difference in MAP of only 10 mmHg had a significant effect on blood loss, but it begs the question whether the lower pressure is necessary, as the difference in blood loss was only 84 mL and both groups had low measured blood losses. Only 6 of the 40 patients received homologous blood transfusions. Recent published series demonstrate that blood loss during THR with normotension varies from 500–1800 mL (Paiement et al. 1987, McMurray et al. 1990, Twyman et al. 1990, Eriksson et al. 1991, Maloney et al. 1991, Planès et al. 1991, Tørholm et al. 1991).

If one plots the mean intraoperative blood loss against the mean intraoperative pressure from a number of publications, one sees a relationship between intraoperative blood loss and MAP (Figure 6). Therefore, any effort to reduce MAP towards 50 mmHg and maintain it throughout surgery, will reduce intraoperative blood loss. Many people believe that, if the pressure is low during surgery, patients will bleed excessively postoperatively. This is not our experience and studies demonstrate that postoperative bleeding is not commoner following hypotension than following normotensive anesthesia (Keith 1977, Thompson et al. 1978, Vazeery and Lunde 1979, Barbier-Böhm et al. 1980, Rosberg et al. 1982, Modig 1988a). Postoperative drainage in our cases (Lieberman et al. 1994) is within the range published by other authors.

Factors affecting blood loss

Arterial pressure is the main factor influencing bleeding during THR but only accounts for 25% of the variance in blood loss during HEA (Sharrock et al. 1993a). It has been suggested that bleeding may also depend on central venous pressure in the wound (Modig 1988c). This may be true during general anesthesia, when ventilation is controlled as higher venous pressure develops (Modig 1988c). However, during THR in the lateral decubitus position, the surgical wound is 6–12 cm above the midsternal line and the venous pressure is usually between 1 and 5 cm of water during HEA. Therefore, venous pressures in the surgical wound during THR under HEA are always subatmospheric which explains why we have observed no relationship between CVP and bleeding. We also found no relationship between intraoperative blood loss and cardiac output or heart rate during HEA (Sharrock et al. 1993c). Other patient variables, including clotting factors, probably account for much

of the variability in intraoperative blood loss at a particular blood pressure.

Advantages of hypotensive epidural anesthesia

Transfusions

Hypotensive epidural anesthesia not only reduces intraoperative blood loss, but is associated with a parallel reduction in transfusion requirements. In a retrospective study of patients receiving THR in 1986 and 1988, patients who had normotensive general or spinal anesthesia and did not donate autologous blood required 1.2 units of homologous blood, whereas those receiving HEA received 0.6 units—a 50% reduction (Sharrock 1993a). Three quarters of the patients having normotensive anesthesia received homologous blood, compared to one-third in the HEA group. In a group of patients who received HEA and did not donate autologous blood, there was a relationship between intraoperative blood loss and the number of homologous units transfused. In addition, there was a significant relationship between the number of units transfused and the calculated preoperative hemoglobin mass. In a subgroup of these patients who did not predonate autologous blood but had a preoperative hemoglobin of 13 gm or more, only one-fifth required homologous transfusions. Patients who required homologous blood tended to have a lower preoperative hemoglobin mass (Sharrock 1993a).

Over 80% of our patients currently predonate autologous blood. In this group, less than 5% receive homologous blood following a primary THR performed with HEA (Sharrock et al. 1993b, Lieberman et al. 1994). Patients undergoing unilateral THR almost never require transfusion intraoperatively. Indications for transfusion have changed so that ,postoperatively, blood is usually transfused to maintain the hemoglobin level above 8 gm, unless there is hemodynamic instability.

Bone cement interface

Hypotensive anesthesia also facilitates optimal penetration of cement into cancellous bone, thereby optimizing fixation of cemented components (Benjamin et al. 1987, Ranawat et al. 1991). In a retrospective case control study assessing the radiographic appearance of cemented acetabular components, improved fixation was noted when HEA was used (20 cases), compared to normotensive general anesthesia (20 cases) (Ranawat et al. 1991). 8 of the patients receiving normotensive anesthesia had radiolucencies, compared to two in the hypotensive group. The overall quality of fixation was ranked as superior in 14 of the 20 patients receiving HEA, but in only one of the 20 patients receiving normotensive anesthesia.

Impact of hypotensive epidural anesthesia on deep-vein thrombosis

Low rates of deep-vein thrombosis (DVT) have been observed with epidural (EA) (Modig et al. 1983b, Modig et al. 1986, Donadoni et al. 1989) or spinal anesthesia (SA) (McCardel et al. 1980, Thorburn et al. 1980, Davis et al. 1989, Wille-Jørgensen et al. 1989), compared to general (GA) anesthesia following total hip surgery. Thorburn observed DVT rates of 53% following GA and 29% following SA (Thorburn et al. 1980). Davis et al. reported a 50% reduction in DVT rate with SA, compared to GA (Davis et al. 1989). Modig noted proximal DVT in 67% with GA and 13% with EA (Modig et al. 1983b). Following surgery for fractured hip, there was a fourfold greater risk of developing a DVT with GA, compared to EA or SA (Sorensen and Pace 1992). These studies all confirm the reduction in DVT following hip surgery using EA and SA (Prins and Hirsh 1990).

Published rates of DVT following THR performed under EA vary from 10 to 55% (Prins and Hirsh 1990, Sharrock et al. 1993b). To define factors which may contribute to this variation, 381 patients undergoing primary THR from 1987 to 1989 by a single surgeon were prospectively studied. All patients received EA and had an operative limb venogram performed on the fourth or fifth postoperative day. The only form of venoprophylaxis was oral aspirin 650 mg daily, elastic stockings, and early ambulation. 15% developed DVT: 3% had proximal DVT and one patient had a clinically symptomatic and verified pulmonary embolus. None died (Sharrock et al. 1993b).

The rate of DVT was related to the duration of surgery. Patients in whom surgery was completed in 70 min or less had a DVT rate of 9%, whereas the rate was 20% when surgery lasted more than 70 min. Rates of DVT were also lower in patients receiving low-dose epinephrine infusion (13%) than in those receiving crystalloid alone (25%) to support blood pressure. Rates of proximal DVT were also lower in patients receiving epinephrine (2.4%) compared to crystalloid (9.3%). Low-dose epinephrine appeared to provide the most benefit in reducing DVT when the surgery lasted over 70 min. In operations lasting over 70 minutes, proximal DVT was observed in 3% using low dose epinephrine, but in 13% when no epinephrine was used (Sharrock et al. 1993b).

Additional studies of rates of DVT using HEA are shown in Table 1. In the first study performed in

Table 1. Thromboembolic disease following total hip replacement under hypotensive epidural anesthesia (HEA) at the Hospital for Special Surgery

Group	n	Proximal clot n (%)	Distal clot n (%)	Pulmonary emboli n (%)	Total thrombo-embolic disease n (%)
Sharrock et al. 1990a					
HEA–aspirin	66	6 (9.1)	9 (13.6)	1 (1.5)	16 (24)
Huo et al. 1992					
Heparin q 30 min	60	1 (1.7)	3 (5.0)	1 (1.7)	5 (8.3)
Heparin-adjusted dose	61	1 (1.7)	3 (4.9)	1 (1.7)	5 (8.3)
Heparin-fixed dose	59	1 (1.7)	5 (8.5)	1 (1.7)	7 (12)
Total	180	3 (1.7)	11 (6.1)	3 (1.7)	17 (9.4)
Lieberman et al. 1994					
Compression boots/ASA	124	0 (0)	7 (5.6)	1 (0.8)	8 (6.4)
Aspirin	126	1 (0.8)	8 (6.3)	1 (0.8)	10 (7.9)
Total	250	1 (0.4)	15 (6.0)	2 (0.8)	18 (7.2)
Huk et al. 1993					
Aspirin	170	6 (3.5)	11 (6.5)	1 (0.7)	18 (11)
Indocin® (indomethacin)	111	2 (1.8)	5 (4.5)	1 (0.9)	8 (7.2)
Coumadin® (warfarin)	59	1 (1.7)	3 (5.1)	0 (0)	4 (6.8)
Total	340	9 (2.6)	19 (5.6)	2 (0.6)	30 (8.8)
Sharrock et al. 1993b					
Aspirin	381	13 (3.4)	45 (12)	1 (0.3)	58 (15)
Total	381	13 (3.4)	45 (12)	1 (0.3)	58 (15)
Grand total	1217	32/1217 (2.6)	99/1217 (8.1)	9/1217 (0.7)	139/1217 (11)
95% confidence interval (%)		1.8–3.2	6.5–9.7	0.3–1.1	9.6–13

1988, DVT was noted in 26% of patients (Sharrock et al. 1990a). Later studies, in which surgery was shorter and low-dose epinephrine was used routinely, noted DVT rates of 10% or less (Huo et al. 1992, Sharrock et al. 1993b, Lieberman et al. 1994). We recently conducted a prospective, randomized trial comparing the effectiveness of HEA, aspirin and external pneumatic compression boots (group I) versus HEA and aspirin alone (group II) in preventing DVT after primary unilateral or bilateral THR (Lieberman et al. 1994). All operations were performed by two senior surgeons, through a posterolateral approach. 231 patients more than 39 years of age were included in the study. There were 113 patients (124 hips) in group I and 118 patients (126 hips) in group II. They all underwent venography on postoperative days 6–8. In group I, there were no proximal thrombi, 7 distal thrombi (66%) and 1 late pulmonary embolus (1%). In group II, there were 1 proximal popliteal thrombus (1%), 8 distal thrombi (6%) and 1 late pulmonary embolus (1%).

In over 1000 cases, the DVT rate assessed with operative limb venography was 11% and the rate of clinical PE was 1%. In-hospital mortality was 0.1% (Sharrock et al. 1995a). Adjunctive forms of thromboprophylaxis combined with HEA do not reduce the rate much more than aspirin alone does: heparin 8% (Huo et al. 1992), coumadin 7%, and boots 7% (Lieberman et al. 1994). We have no data on DVT rates using low molecular weight heparin with HEA.

Cost benefit

The technique is somewhat more complex, requiring an arterial catheter, an additional infusion pump and, in selected patients, a central venous catheter. These require time to set up, which adds to the cost of the procedure (about US$ 20, excluding the central venous catheter). On the other hand, the potential benefits include fewer perioperative transfusions, less intravenous fluid, improved cement fixation, and a simplified protocol for deep-vein thrombosis prophylaxis. In addition, it is not necessary to use cell-savers intraoperatively when using HEA. In spite of the additional cost and delay, we believe that this technique is cost-effective.

Aspirin

The efficacy of aspirin in reducing thromboembolism following THR has been controversial. At the Hospital for Special Surgery, aspirin has been the drug of choice following THR since the mid-1970s (Salvati and Lachiewicz 1976). Two recent studies have shown the efficacy of aspirin in reducing thromboembolism following THR. Alfaro et al. (1986) demonstrated that aspirin reduced circulating platelet aggregates and Powers et al. (1989), in a randomized

trial, compared the effect of aspirin and warfarin in the prevention of DVT following surgery for fractured hip. Aspirin was equally effective in reducing proximal clots and pulmonary embolus. Recently, a meta-analysis has shown aspirin to be a beneficial form of thromboprophylaxis, following general and orthopedic surgery (MacMahon et al. 1994). Furthermore, postoperative administration of aspirin has significantly reduced the incidence of ectopic ossification following THR, as compared to coumadin (Pagnani et al. 1991).

Aspirin in combination with HEA has a number of advantages. It is cheap, easy to administer, can be continued readily following discharge, does not require monitoring of prothrombin time, nor require intramuscular injection (as with low-molecular weight heparin). In addition, major bleeding episodes are infrequent (MacMahon et al. 1994).

How hypotensive epidural anesthesia reduces DVT

Venous thromboembolism occurs in a setting of venous stasis and is accelerated by either a hypercoagulable state or by injury to the venous endothelium (Virchow's triad) (Thomas 1985). Studies in animals have demonstrated that when flow through a vein stops, adherence of leukocytes and platelets to venous endothelium develops within minutes, if there is trauma to the vein, but is minimal without venous trauma (Stewart 1993). The adherence of leukocytes and platelets to the endothelium provides the nidus for propagation of a thrombus. Hypoxia develops with prolonged venous stasis, which also appears to promote the adhesion of leukocytes and platelets to the endothelium (Malone and Morris 1978, Ogawa et al. 1990).

All three components of Virchow's triad exist during THR. Twisting and kinking of the femoral vein occurs during flexion and internal rotation of the leg during surgery on the femur. This leads to obstruction of the femoral vein and creates stasis (Stamatakis et al. 1977, Binns and Pho 1990, Planès et al. 1990). With reaming of the femur and insertion of the prosthetic component and methylmethacrylate; fat and bone marrow, containing tissue thromboplastin, are released into the venous circulation which is stagnant at the level of the obstructed proximal femoral vein (Modig et al. 1975, Orsini et al. 1987, Ereth et al. 1992). In addition, injury to the wall of the femoral vein occurs due to surgical trauma around the hip and the prolonged twisting of the vein (Stamatakis et al. 1977).

Studies of circulating markers of thrombosis, conducted in 46 patients undergoing primary THR, showed little evidence of thrombogenesis during femoral dislocation, femoral osteotomy, reaming of the acetabulum or insertion of a cemented or noncemented cup (Sharrock et al. 1995b). However, there was a 3–5-fold progressive increase in each of the markers of thrombosis (fibrinopeptide A, thrombin-antithrombin III complexes, and prothrombin fragment F1+2) during placement of the femoral component. This demonstrates that the period of maximal thrombogenesis occurs during femoral preparation and insertion of the femoral component (particularly if cemented) and confirms previous observations that the combination of femoral venous occlusion, trauma to the femoral vein and entry of tissue thromboplastin into the femoral vein are the main thrombogenic factors contributing to DVT during THR.

An understanding of the pathogenesis of DVT during THR provides a basis for the prevention of DVT. First, any maneuver which limits the duration of femoral venous occlusion should minimize venous stasis and reduce the likelihood of developing DVT. As mentioned, when surgery is longer, DVT rates are higher (Sharrock et al. 1993b). Furthermore, we noted a relationship between the duration of reaming the femur and an increase in the prothrombin fragment F1+2 level, suggesting a relationship between the duration of femoral venous occlusion and thrombin generation (thrombogenesis) (Sharrock et al. 1995b). Surgical technique can be modified to limit the duration of femoral venous occlusion. For example, the leg can be put in neutral while waiting for the femoral cement to be ready. Hypotensive epidural anesthesia, by reducing overall blood loss, shortens the duration of surgery, as the time spent in controlling bleeding is significantly reduced and consequently also the DVT rate (Lieberman and Geerts 1994).

Other surgical maneuvers may reduce the amount of tissue thromboplastin entering the circulation. Pulse lavage (Byrick et al. 1989) thoroughly cleans the femoral canal and a well-fitting cement restrictor limits pressurization of the distal femur (Patterson et al. 1991). Hypotensive epidural anesthesia, by reducing blood loss and facilitating a dry femoral canal, may act in the same way as pulse lavage to limit entry of thromboplastin into the circulation.

How can the use of epinephrine reduce the DVT rate? Epinephrine significantly increases skeletal muscle blood flow during HEA (Bading et al. 1994). The increased flow during surgery could reduce stasis to a sufficient extent to prevent thrombogenesis.

However, femoral venous occlusion and stasis are probably inevitable during during work on the femur, even though epinephrine may reduce it (Sharrock et al. 1995b). It is also possible that epinephrine has a direct effect on the interaction between endothelial cells, leukocytes and platelets (Bazzoni et al. 1991). Low-dose intravenous epinephrine does not enhance fibrinolysis during THR (Sharrock et al. 1992).

Minimizing intraoperative blood loss by hypotension may reduce DVT by several mechanisms (Lieberman and Geerts 1994). First, perioperative disturbances in coagulability are, in part, related to perioperative blood loss (Andersson et al. 1987, Murray et al. 1995). Intraoperatively, there is a reduction in circulating anticoagulants, such as antithrombin III (as well as other circulating factors), due to hemodilution and consumption (Gitel et al. 1979, Donadoni et al. 1989, Francis et al. 1989). Postoperatively, the rebound in factor VIII levels, etc., which produces the hypercoagulable state is also related to the degree of blood loss (Modig et al. 1983a). Secondly, if too much intravenous fluid or blood is infused during surgery to replace excessive blood loss, hypothermia may develop. This results in peripheral vasoconstriction, leading to venous stasis in the extremities thereby predisposing to DVT.

Finally, short-acting low-dose anticoagulants can be administered during surgery on the femur to limit the activation of the clotting cascade during this period of maximal thrombogenesis. 1000 units of unfractionated heparin administered intravenously prior to work on the femur suppressed the rise in fibrinopeptide A levels, demonstrating that this may be an effective adjunctive form of thromboprophylaxis during THR, particularly for high-risk patients (Sharrock et al. 1995b). Intraoperative heparin is associated with a DVT rate of 8% and a proximal DVT rate of less than 2%, without an increase in bleeding complications (Huo et al. 1992).

Conclusion

Hypotensive epidural anesthesia is a technique for safely lowering MAP to 50 mmHg during surgery by combining an extensive epidural blockade and an intravenous infusion of low-dose epinephrine. Hemodynamically, it is associated with preservation of central venous pressure and cardiac output. The technique is associated with a low intraoperative blood loss, which shortens the duration of surgery, a reduction in perioperative transfusion requirements, improved fixation of cemented components, and a low rate of DVT. The technique is safe for the vast majority of candidates for THR, including elderly patients. In-hospital mortality at our institution is 0.1% (Sharrock et al. 1995a), i.e. well below the national average.

Acknowledgments

This study was funded by the Hospital for Special Surgery, Department of Anesthesiology Research Fund, by the generous support of Ms. Emma A. Daniels, President of the May Ellen and Gerald Ritter Foundation, and Dr. and Mrs. Gianbattista Foglia.

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