Bahrain Medical Bulletin, Volume 17, Number 4, December 1995

PERIOPERATIVE EVALUATION AND MANAGEMENT IN THE ELDERLY

A. Abyad, MD,MPH,AGSF*

Perioperative assessment in the elderly is important since they present challenging medical situations. The assessment involves identifying coexisting disease, defining the urgency of the intervention, and anticipating postoperative complications based on the type of the surgery. The role of the physicians is searching for correctable conditions, and avoiding complication during or after the operation. Bahrain Med Bull 1995;17(4):

The geriatric patient present the physician with several challenges in the operative and postoperative period due to several interacting factors including, prevalence of co-existing morbidity, age-related decline in physiologic parameters, the wide spectrum of surgery which these patients undergo, increased morbidity and mortality associated with surgery in the aged, and historical bias against surgical intervention. The associated diseases and urgency of the procedure have been more important factors than age in predicting mortality. Despite this, a fatality rate of 0.7 % within 48 hours of elective surgery is expected in those older than 90 years (Table 1)[1,2].

Table 1
Peri-operative mortality for selected elective surgical procedures

Procedure	All Adults %	Older Persons %
Hernia repair	0.01	0.3
Mastectomy	0.1	0.6
Cholecystectomy	1.0	5.0
Pneumonectomy	5.0	15.0
Coronary artery bypass	2.0	5.0

An elderly differs from a younger patient who is undergoing surgery in the increased probability of developing complications subsequent to the procedure. Many postoperative complications can be detected if the physicians caring for the patients are vigilant. One of the greatest difficulties in an early diagnosis of postoperative

* Assistant Professor
Department of Family Medicine
American University of Beirut
Lebanon

complications in older patients is appreciating that a change in a patient's status has, in fact, happened. This difficulty is increased if different physicians assume responsibility for the preoperative and postoperative period.

Management

There are basically several issues in the management of high-risk elderly patients. Induction of anaesthesia, marks the initiation of the second phase of monitoring which is preceded by the preoperative evaluation. The third phase is represented by postoperative care and recovery. In order to enhance outcome from surgical management of elderly patients and to avoid errors, several rules need to be followed: (1) careful preoperative evaluation and preparation, (2) appropriate anaesthesia and physiological monitoring during the operative

procedures, (3) recognition of alterations in clinical pharmacology, (4) minimization of postoperative stresses of hypothermia, hypoxemia and pain, (5) prevention of alterations in blood pressure and heart rate, (6) avoidance of disturbances of fluid, electrolyte and acid-base status and (7) surgical technique.

Intra operative Concern

The choice of the advantages and disadvantages must be weighed in each individual case. Local anaesthesia is generally safe, and may be used in procedures such as cataract or dental/oral surgery, or surgery involving the extremities. Regional anaesthesia is often used for hernia repair, hip surgery, vaginal hysterectomies and transurethral resection of the prostate. Despite common belief, there is no evidence of a decrease in respiratory complication with regional as opposed to general anaesthesia. Regional anaesthesia can also be associated with significant haemodynamic effects, including hypotension and decreased cardiac output. Studies comparing postoperative mental changes between patients after regional or general anesthesia vary in their conclusions; some have found less confusion after regional anesthesia and others have shown no difference[3,4].

General anaesthesia should be used in major abdominal and thoracic procedures, when control of the airway is essential and when the patient cannot comply with instructions. Most general anaesthetics will depress myocardial function to greater or lesser degree, with variable effects on heart rate and the peripheral vasculature. Some of these effects are influenced by medications, such as B-blockers and antiarrhythmic agents, and the anaesthetist needs to be informed of all drugs the patient has been taking before surgery[3,4]. The effects of general anesthesia may be prolonged if the patient becomes hypothermic in the operating room. This is a dangerous occurrence in elderly patients as they are most susceptible both to the development of hypothermia and its consequences[3,4].

Other risk factors for hypothermia include operations longer than 3 hours, exposure of the major body cavities, and major vascular surgery. The hypothermic patient is more susceptible to cardiac arrthymias, congestive heart failure and pneumonia. Peripheral vasoconstriction while hypothermic can cause hypertension in the operating room, and vasodilatation that occurs when the patient is rewarmed can cause significant hypotension. Shivering as the patient awakens from anaesthesia can also be dangerous, as it dramatically increases oxygen demand. Hypothermia can be avoided by careful monitoring of core temperature, warmer operating rooms, warming blankets and intravenous fluids given at body temperature.

Another risk to the elderly patient is development of decubitus ulcers while lying on a hard operating table for a long time without movement. Proper padding of the table and intermittent relief of pressure on bony prominences can avoid this problem.

Anaesthesia and Cardiac Arrhythmias

Ideally, anaesthesia permits safe, efficient and stress-free performance of a surgical procedure and a rapid, uneventful return to normal function. Special concerns in the elderly patient are (1) avoidance of haemodynamic instability, (2) maintenance of a favourable myocardial oxygen supply-demand ratio and (3) minimization of postoperative alterations in mental function. The strong relation between intra operative hypotension and postoperative morbidity and mortality has been well established[5]. For example, when mean blood pressure decreases from preoperative values by one-third or more for 10 minutes or longer, the risk of cardiac death is increased five-fold[5,6,7]. Intra operative tachycardia is also associated with myocardial ischemia. The combination of

tachycardia and hypotension may be particularly hazardous in the elderly patient[5,6,7].

In a recent study8, an anaesthesia follow-up programme (100,000 anaesthetics) and vital statistical data were used to assess the role of anaesthesia in operative deaths. Four factor groups relating to the patient-surgical procedure, the anaesthesia and other parameters were assessed by logistic regression analysis to ascertain which variables were predictive of 7-day mortality. Advanced age, male gender, physical status, major surgery, emergency procedure, intra operative complications, narcotic techniques and administration of one or two drugs as opposed to many drugs (few side effects of each preparation) were associated with increased mortality. Duration of anaesthesia, experience of the anaesthesiologist and inhalation techniques were not associated with increased mortality. The conclusion of this study was that patient and surgical risk factors were much more important in predicting 7-day mortality than were anaesthesia factors. A high preoperative physical status score based on the American Society of Anaesthesiologists scoring system, an emergency operation or a major surgical procedure placed patients at a very high risk of dying. Arrhythmias often occur during anaesthesia and surgery as well as in the early postoperative period. Vanik and Davis9 reviewed the electro cardiographic records of 5,013 anaesthetic patients and found the incidence to be 16.3% in individuals with no known preoperative arrhythmias, 26.6% in those with known preoperative arrhythmias and 34.4% in those with known preoperative heart disease, yielding a mean incidence of 17.9%.

Other studies have found rates as high as 60 to 70%10,11. Twenty to thirty percent of arrhythmias occur during the induction of anaesthesia. Atrioventricular dissociation, premature ventricular contractions and sinus tachycardia are the most commonly encountered arrhythmias[12]. Patients with pre-existing cardiac disease and decreased cardiac reserve are particularly likely to develop arrhythmias. Arrhythmias tend to occur with increasing frequency in individuals of increasing age. If only patients without clinical evidence of heart diseases are considered however, there is no real difference between age groups in the incidence of anaesthesia-relating arrhythmias[12,13].

Characteristics of arrhythmias that lead to haemodynamic instability include a rapid ventricular rate, a prolonged duration of the abnormality, a disjointed temporal relation between atrial and ventricular activity and an exaggerated autonomic nervous system response[14]. Thus, atrioventricular (AV) conduction disturbances and ventricular arrhythmias are potentially the most serious. In general, anaesthetic agents are direct myocardial depressants[5]. In addition, certain agents (especially cyclopropane, chloroform, halothane, methoxyflurane and trichloroethylene) have the property of sensitising the myocardium to catecholamines, thus lowering the threshold for ventricular tachyarrhythmias. Surprisingly, the reported incidence of arrhythmias with regional anaesthetics does not differ significantly from that with inhalation agents, although there is a higher rate of occurrence in intubated patients[10,12].

Initial treatment of arrhythmias should be directed at prompt correction of specific electrolyte imbalances (primarily disorders of potassium metabolism), hypoxemia, hypercapnia and acid-base abnormalities. Usually it is not possible to identify a correctable underlying basis for the arrhythmia and specific antiarrhythmic drugs are required.

The presence of arrhythmias does not always necessitate intervention; the decision to treat specific rhythms will depend on the ability of the patient's cardiovascular system to tolerate them. With the exception of certain ventricular ectopic beats occurring in patients with recent myocardial infarction or known extensive cardiac disease, ectopic beats usually do not require treatment[5,15]. Patients with arrhythmias that affect cardiac output should also be treated.

Respiratory Care

There is a predisposition for micro and macro atelectasis (V/Q mismatch) and hypoxemia, and elderly patients are at particular risk for postoperative respiratory complications. There is also a predisposition to aspiration due to changes in mentation and loss of gag reflex. In the postoperative period, central nervous system depression associated with anaesthesia or analgesics, combined with prolonged periods of bed rest, compounds these changes with the all-too-frequent result of aspiration pneumonia. Extended inactivity in elderly surgical patients may also encourage venous stasis and subsequent pulmonary embolism. Respiratory assessment includes a history, physical examination, and chest X-rays[1,4]. The history should focus on the usual level of activity, smoking, presence of dyspnea, and previous deep vein thrombosis or pulmonary embolus. It was noted that there is at least a two-fold greater risk of pulmonary complications in patients with a positive history of smoking or pre-existing pulmonary disease[1,4]. In another study, it was found that in 100 consecutive elective surgery patients of 70 years or older, abnormalities were found in 10 to 27 patients who had no specific indication for chest X-rays[2,3]. Simple spirometry is useful as a screening test in patients with suspected obstructive lung disease, patients undergoing thoracic or abdominal surgery and in those who are obese, smoke or are older than 70 years[4,16]. An arterial blood gases analysis is required in patients with significantly abnormal spirometry[16].

Several studies have sought to determine whether routine prolonged postoperative ventilatory support is helpful in the elderly or high-risk patient[4,16]. There is no evidence, however, that a mandatory period of mechanical ventilation decreases morbidity or mortality. Elderly patients would therefore be extubated when standard criteria are met. Once extubated, aggressive physiotherapy which emphasises sustained inspiratory effort using incentive spirometry is most effective in the prevention of complications. Small doses of narcotics sufficient to decrease incisional pain without causing obtundation are useful in the achievement of an effective cough. Humidification of inspired air and frequent nasotracheal suctioning should be used in those patients with feeble cough effort.

The simplest and most effective method to decrease postoperative atelectasis and venous stasis is early mobilisation and ambulation. Patients over 60-years old have a 25% incidence of pulmonary embolus as the primary cause of death, compared to a 3% incidence for patients under 50 years old[17]. Several factors need to be considered during the postoperative period in order to avoid respiratory complications. Early resumption of physical activity, adequate analgesia, incentive spirometers, breathing exercises and intermittent positive-pressure breathing are all necessary components of postoperative care. Additionally, supplemental oxygen via mask or prongs should be provided to elderly patients following major thoracic and abdominal procedures.

By encouraging early physical activity one avoids the closure of small airways in dependent areas of the lung associated with the supine position. In this way, poor gas exchange, decreased functional residual capacity, ventilation perfusion mismatches, increased alveolar-arterial gradients and hypoxia are avoided[18,19].

Epidural or subarachnoid anaesthesia below midthoracic levels interferes much less with normal respiratory function than does general anaesthesia. Epidural narcotics or local anaesthetics are associated with partial reversal of decreased vital capacity and functional residual capacity and are superior to parenteral narcotic analgesia[16].

Diaphragmatic and pulmonary functions begin to improve 24 to 48 hours after upper abdominal surgery[20]. In one study, preoperative dyspnea at rest and arterial hypoxemia were the best predictors of the need for postoperative

mechanical ventilation in patients with an FEV1 of less than 1 L[21]. Age was not significant when these factors were taken into account. Despite the potential benefits of prophylactic mechanical ventilation, the impairment of pulmonary defenses associated with endotracheal intubation and ventilation and the potential for development of respiratory infection and ventilator dependence increase with time; early weaning is therefore indicated.

Postoperative Cardiovascular Monitoring

It is in the first 48 to 96 hours after operation that the most significant shifts in fluid between body compartments occur, the onset of congestive heart failure is most frequent, and the haemodynamic abnormalities contributing to myocardial ischemia are most readily identified and treated[6,22]. When invasive haemodynamic monitoring has been initiated preoperatively or in the operating room, consideration should be given to continuing postoperatively. In studies of patients of varying ages, myocardial infarction (MI) and reinfarction have tended to occur in the early postoperative period, often painlessly. Continuous monitoring of ST segment changes in the postoperative period may prove to be a sensitive method for detecting myocardial ischemia and determining whether intensive therapy is needed. Data and observations from many studies suggest the need for frequent clinical assessment and continuous electrocardiographic monitoring for at least 3 days and possibly as long as 6 days postoperatively in elderly patients who are at high risk for postoperative cardiac complications[6,22]. At present, serum creatinine kinase (CK) determinations can be used to diagnose a perioperative MI. Serum CK-MB bands in excess of 5% of the total serum CK, or more than 50 IU/L of plasma, are diagnostic of acute perioperative MI. These criteria are especially good when the determinations are performed 18 to 30 hours after surgery. The diagnosis of infarction can be confirmed by two relatively simple means; serial 12-lead ECGs and analysis of serum lactate dehydrogenase levels. If the ratio of lactate dehydrogenase-1 to lactate dehydrogenase-2 is greater than 1, the diagnosis of acute perioperative MI is confirmed. The sensitivity and specificity of these tests approach 99% if the two separate CK-MB determinations, performed 18 to 30 hours postoperatively, meet either the 5 percent or 50 IU/L criteria[23-25].

Pain Control

Adequate pain control should be a goal for the comfort of the patient, and to prevent postoperative complications by facilitating early mobilisation, coughing and deep breathing. Assessing the need for medication against pain may be difficult in demented or delirious patients, as they may not remember or know how to ask for medication. Pain in these patients may be manifested by agitation or increased confusion rather than by complaints of discomfort. On the other hand, overmedication can also be manifested by increased confusion[2].

There are many analgesics available for use in postoperative pain. Narcotics are very effective, but their prolonged half-lives in the elderly patient can lead to accumulation, and constipation and nausea are common side-effects. They should initially be given regularly rather than on demand as this will improve pain relief and reduce the total dose needed. The same results can be obtained in those who are mentally intact by patient-controlled analgesia, which allows them to administer their own medication through a bedside pump and has been shown to be useful even in the frail and elderly patient. Epidural analgesia can be very effective, with fewer systemic effects. For less severe pain, non-steroidal anti-flammatory agents or Paracetamol can be helpful. Another option is a trascutaneous electrical stimulation unit, which has been used successfully on elderly patients and avoids the many untoward side-effects of medication.

Prophylaxis Against Venous Thrombosis

Patients of any age undergoing surgery, particularly orthopaedic cases, are at risk of developing deep venous thrombosis. Fibrinogen scanning has detected thrombosis in the legs in a quarter of general surgical patients with 1.6% developing clinically significant pulmonary embolism (Consensus Conference 1986). The risk is highest in hip surgery and knee reconstruction with 45 to 70% of patients for hip surgery developing a pulmonary embolism. Predisposing medical conditions include heart failure, acute myocardial infarction, cancer, obesity and stroke with weakness of the legs.

There are various ways of preventing deep venous thrombosis and pulmonary embolism; their use should be routine in elderly patients in whom there are no contraindications. The incidence of both conditions in the general surgical patient has been significantly reduced by the use of low-dose subcutaneous heparin. Giving heparin 2 hours before surgery and every 8 to 12 hours after, cuts the incidence of deep venous thrombosis to 10% and of embolism to 0.8%. Other regimens used to prevent venous thrombosis include dihydroergotamine / heparin combinations, and adjusted dose heparin therapy. Dihydroergotamine is alpha-adrenergic blocking agent that stimulates the vascular smooth muscle. Adding this agent to heparin augments the prophylactic effect, but the vasoconstriction it induces may cause complications in those patients with vascular disease. In patients undergoing hip surgery, adjusted-dose heparin has been shown to be superior to the standard heparin regimen. Adjusting the dose of heparin, to keep the activated partial thromboplastic time between 31.5 and 36 s, decreased the incidence of proximal deep-vein thrombosis from 32% in those treated with fixed dose heparin to 5%.

Warfarin can also be used, beginning 1 to 2 days before surgery and continuing until the patient is fully able to walk. In elective surgery, two-step warfarin therapy is preferred by some. In this treatment, the patient's prothrombin time is maintained at 2 to 3 s longer than the control for 10 to 14 days before surgery, and at 1.5 times the control after surgery.

Non-pharmacological methods of prophylaxis are also available. Properly fitted, graduated, elastic compression stockings improve venous return and can be used in combination with other therapies. The use of an external pneumatic compression stocking is a new technique. It should begin before surgery and continued at least 3 days or until the patient is fully ambulatory. This may be the preferred approach in patients who are at significant risk from bleeding with anticoagulation.

Delirium

Delirium is a common complication in surgical patients occurring in 10 to 15% of all ages, and often in older patients. Studies of elderly patients with hip fractures have shown that up to 61% develop postoperative confusion. The occurrence of delirium is associated with prolonged stays in hospital, more needed for long-term care after discharge, a decreased ability to walk, falls, and a higher incidence of postoperative complications and death. Besides age, risk factors include dementia, depression, Parkinson's disease, impaired hearing or vision, anti cholinergic drugs, emergency surgery, previous psychiatric conditions and medical problems. Knowledge of preoperative mental status is important in order to detect subtle changes that may indicate the presence of delirium.

The best approach to the problem of delirium is to try to prevent it. Keep the patient oriented by visual and verbal cues, by ensuring they have their glasses or hearing aids and by allowing them some familiar objects from home. Medications should be kept to a minimum and their side-effects carefully monitored.

If delirium does occur, management consists of orientation techniques described above and discontinuation or decrease in the dosage of any medications that might be implicated. If the patient is agitated, violent or hallucinating, psychotropics, such as haloperidol at their lowest effective dose, can be helpful. If the agitation is related to alcohol withdrawal, it should be treated with a short acting benzodiazipine although chlormethiazole may be preferred in countries where it is available. Increasing numbers of cases of delirium in elderly patients are due to withdrawal of benzodipine hypnotics or tranquillisers.

Other Postoperative Concerns

These include urinary incontinence or retention, constipation and decubitus ulcers. Being aware of the risk factors and instituting preventive measures may decrease the frequency with which they occur.

Urinary problems are common in elderly patients in hospital with a prevalence of 17% on the general surgical ward in one study[2,26]. Medication, immobility, faecal impaction and sedation, all common factors postoperatively, can each increase the incidence of incontinence. Adverse consequences include decubitus ulcers, falls and the insertion of indwelling catheters with their attendant risk of infection. The chances of a patient remaining continent can be enhanced by the provision of a urinal and/or bedside commode, regular toileting, and avoidance of constipation, oversedation and unnecessary use of drugs that might induce continence. Indwelling catheters should not be used for the management of incontinence unless there is skin breakdown or urine output needs to be monitored closely.

Postoperative urinary retention is also a common problem. Many anaesthetic agents can induce retention by altering the effect of the autonomic nervous system on the bladder and urethra. Older men are especially at risk owing to high prevalence of urethral narrowing from prostatic hypertrophy. Indwelling catheters are commonly used intraoperatively, and when used 24 hours after orthopaedic surgery they have been shown to decrease the incidence of postoperative retention as compared to intermittent catheterisation. Unless absolutely necessary for management of fluid status, they should be removed 24 to 48 hours after surgery.

Both urinary incontinence and retention can be induced by faecal impaction. Constipation is extremely common after surgery, owing to direct affects of surgery on the bowel. Early mobilisation

Geriatric Surgery

As with younger patients, choosing the appropriate option for surgical management is often a bigger problem for today's surgeons than the skill and resources needed to carry out standard procedures safely. For example, conservative management of small rectal cancers by electrocoagulation with or without adjuvant radiotherapy, or with endocavitary irradiation, has an important role in elderly patients who may find a colostomy very difficult to manage. And some very elderly women with Stage I and Stage II breast cancer are now being managed with Tamoxifen only, without removing the cancer, when any operation seems unnecessarily risky.

Finally, it is unfortunate that the use and abuse of endoscopic surgery in the abdomen, as for cholecystectomy, is not discussed. The geriatric consultant should not discourage well planned elective surgery because of age. This is especially true of the "aged well" without cardiac risk factors. Delaying needed surgery solely because of age, only to have the procedure done later as an emergency, is a disservice due to the added risk of emergency surgery. It is

worth emphasising that at the age of 70-years, the remaining life expectancy is 10-15 years.

On the other hand, physicians should not take for granted the "appropriateness" of major, (eg carotid endarterectomy) or minor, (eg cataract) geriatric surgery. Thus the physician should determine that the proposed surgery will actually benefit the patient.

Because age may alter clinical manifestations, geriatric patients require meticulous preoperative assessment to uncover occult disease.

Attention to detail, such as antiembolism prophylaxis, can have a major impact upon reducing complications and/or death.

Because complications may evolve over days postoperatively, geriatric patients require careful postoperative follow-up to detect complications and prevent iatrogenic morbidity.

CONCLUSION

As the population continues to age and surgical perioperative technique continue to improve, the number of elderly undergoing surgery will increase. Comprehension of the physiology of ageing and knowledge of associated conditions, in combination with careful monitoring and postoperative management, can assure a good outcome for the vast majority of these patients.

REFERENCES

1. Garibaldi RA, et al. Risk factors for post-operative pneumonia. Am J Med 1981;70:677.

2. Milamed DR, Hedley-Whyte J. Contributions of the surgical sciences to a reduction of the mortality rate in the United States for the period 1968 to 1988. Ann Surg 1994;219:94-102

3. Tornebrandt, K, Fletcher R. Preoperative chest X-rays in elderly patients. Anaesthesia 1982;37:901.

4. Celli BR. What is the value of preoperative pulmonary function testing? Med 1994;331:25-30.

5. Goldman L. Assessment of perioperative cardiac risk. N Engl J Med 1994;330:707-9.

6. Rao TL, Jacobs KH, El-Etr AA. Reinfarction following anaesthesia in patients with myocardial infarction. anaesthesiology 1983;59:499.

7. Charlson ME, MacKenzie CR, Gold JP et al. The preoperative and intraoperative haemodynamic predictors of postoperative myocardial infarction or ischemia in patients undergoing noncardica surgery. Ann Surg 1989;210:637.

8. Cohn MM, Duncan PG, Tata RB. Does anaesthesia contribute to operative mortality? JAMA 1989;260:2859.

9. Vanik PE, Davis HS. Cardiac arrhythmias during halothane anaesthesia. Anaesth Analg 1968;47:299.

10. Katz RL, Bigger JT. Cardiac arrhythmias during anaesthesia and operations. Anaesthesiology 1970;33:193.

11. Poldermans D, Fioretti PM, Forster T, et al. Dobutamine stress echocardiography for assessment of perioperative cardiac risk in patients undergoing major vascular surgery. Circulation 1993;87:1506-12.

12. Dodd RB, Sims WA, Bone DJ. Cardiac arrhythmias observed during anaesthesia and surgery. Surgery 1962;41:440.

13. Baron JF, Mundler O, Berttrand M, et al. Dipyridamole- thallium scintigraphy and gated radionucliotide angiography to assess cardiac risk before abdominalaortic surgery. N Engl J Med 1994;330:663-9.

14. Samet P. Haemodynamic sequelae of cardiac arrhythmias. Circulation 1973;47:399.

15. Philbin DM, Hutter AM. Intraoperative cardiac rrhythmias. Int Anaesthesiol Clin 1978;17:55.

16. Zibrak JD, O'Donnell CR, Marton K. Indications for pulmonary function. Ann Intern Med 1990;112:763-71.

17. Morrell MT. Nunhill MS. The post-mortem incidence of pulmonary embolism in a hospitalised population. Br J Surg 1968;55:347.

18. Craig DB, Wahba WM, Don HF, et al. "Closing Volume": and its relationship to gas exchange in seated and supine positions. J Appl Physiol 971;31:717.

19. Vaughn RW, Wise L. Postoperative arterial blood gas measurement in obese patients: effect of position of gas exchange. Ann Surg 1975;182:705.

20. Ford G, Whitelaw W, Rosenal TW, et al. Diaphragm function after upper abdominal surgery in humans. Am Rev Respir Dis 1983;127:431.

21. Nunn JF, Milledge JS, Chen D, et al. Respiratory criteria of fitness for surgery and anaesthesia. Anaesthesia 1988;43:543.

22. Deron SJ, Kotler MN. Noncardiac surgery in the cardiac patient. Am Heart J 1988;116:831.

23. Montamat SC, Cusack BJ, Vestal RE. Management of drug therapy in the elderly. N Engl J Med 1989;321:303.

24. Greenblatt DJ, Sellers EM, Shader RI. Drug therapy: drug disposition in old age. N Engl J Med 1982;306:1081.

25. Schmucker DL. Alterations in drug disposition. In Stephens CR, Assaf RA (eds). Geriatric anaesthesia: principles and practice. Stoneham MA, Butterworth 1986;155.

26. Novis BK, Roizen MF, Aronson S, et al. Association of pre-operative risk factors with postoperative acute renal failure. Anesth Analg 1994;78:143-9.