Physiologic and Anesthetic Considerations in Octogenarians Undergoing Laparoscopic Partial Nephrectomy

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The number of small renal tumors detected is increasing as imaging becomes both more available and advanced, and as the population ages, with a greater proportion of patients in their 80s emerging with small and treatable renal tumors. The technique of laparoscopic partial nephrectomy is emerging and becoming ever more popular in some centers, and is potentially a safer alternative for the elderly due to improved postoperative pain, shorter hospital stay with faster return to preoperative activities, and lower rates of morbidity and mortality. We present a systematic review of the physiologic and anesthetic considerations in octogenarians undergoing the procedure, highlighting special considerations and the need for expertise throughout the multidisciplinary team when dealing with these patients, in order to minimize risk and optimize outcome.

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KEY WORDS

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In the United Kingdom, life expectancy is increasing, with a significant increase in the "oldest old." Data from the Office of National Statistics shows that, in 2010, the percentage of the population over age 85 years has doubled from 1% to 2% overall, and by 2035, is estimated to be at 3.6 million, or 5% of the total population.[1] In 2010, there were a total of 670 new diagnoses of renal cell carcinoma (RCC) overall (ICD-10 code C64) in 80- to 84-year-olds, and 639 in those over age 85 years, which is 19% of the total new diagnoses across all ages.[2] Despite technologic advances in treatment, the death rate attributed to

RCC has been on the rise, with an increase of 21% in those aged 80 to 89 years between the years 2007 and 2010 alone.[3]

Traditionally, radical nephrectomy (RN) was the treatment of choice for RCC in patients with a normal contralateral kidney,[4] and partial nephrectomy (PN) reserved for those for whom nephron sparing is necessary.[5] Due to advanced imaging techniques, however, lower stages of RCC are being found at initial diagnosis,[5] and this, coupled with advancing surgical technique and experience, allows for the consideration of PN in more cases than ever before. It has now been demonstrated that PN confers equivalent cancer control as RN for T1 tumors (< 7 cm), and where technically feasible, for T1b tumors.[6] Furthermore, PN has been shown to improve global survival when compared with RN for equivalent tumors, whereby a recent study by Weight and colleagues[7] found that, when looking at both cancer-specific survival and loss of renal function and associated death from any cause in patients with T1b disease undergoing PN versus RN, cancer-specific survival was equivalent, and loss of renal function was substantially higher in the radical group. Postoperative renal insufficiency was also shown to be a significant independent predictor of cardiovascular-specific survival, and within the radical group, the loss of renal function was associated with a 25% increased risk of cardiac death and a 17% increased risk of death from any cause.

Although open partial nephrectomy (OPN) now forms the reference standard for these smaller tumors due to preservation of renal function, laparoscopic partial nephrectomy (LPN) is now offered as an alternative. Aside from the well-established benefits of laparoscopic surgery such as reduced postoperative pain, reduced hospital stay, and improved cosmetic appearance, other benefits may arise specific to the elderly. The use of LPN seems to be center-dependant and evolving; therefore, randomized, controlled trials are yet to take place for comparison of safety and long-term outcomes.

Several retrospective studies have taken place. Inderbir and colleagues[8] found that, despite differing patient groups when comparing postoperative outcomes of OPN (n = 1028) versus LPN (n = 771), the LPN group experienced shorter operative time, decreased intraoperative blood loss, and shorter hospital stay. These findings were similar to those of Sun and associates,[9] who provided a retrospective national cohort analysis over a 9-year period, showing not only that the use of LPN increased 19-fold over this period, but the need for blood transfusions, length of hospital stay, and in-hospital mortality were all lower.

There are significant ethical considerations to be made in the decision to perform any operation in the group deemed elderly, and denying gold-standard surgery simply on the grounds of age and presumed risk rather than carefully balanced risk:benefit analysis, coupled with patient choice, will surely cause debate. For example, a relatively recent study analyzing patients from the Surveillance, Epidemiology, and End Results (SEER) database showed that relative to nephrectomy, nonsurgical therapy was associated with an almost sixfold increase in cancer-specific mortality, independent of age.[10] However, by age 80, it is likely that ≥ 1 comorbidity will be present, with one study showing that, of all patients over age 80 undergoing urologic surgery in a single center, 88.3% had ≥ 1 comorbidity.[11]

Although the assumption that the elderly have decreased physiological reserve may be correct,[11] assuming perioperative morbidity and mortality will be proportionately high in renal surgery may not be.[12] Several series have shown that perioperative mortality is unexpectedly low, between 0 and 2%,[13,14] and morbidity is low or certainly acceptable across RCC surgery in general. A study by Staehler and colleagues[13] found overall complication rates in a series of 379 surgical resections for renal tumors in patients aged > 75 years for RN, PN, and radical nephroureterectomy to be 12%, 15%, and 20%, respectively. Another by Berdjis and colleagues[14] found that, although morbidity and mortality correlated with American Society of Anesthesiologists (ASA) score—the most commonly used physical status stratification system—it did not correlate with age.

This article does not attempt to discuss the indications for operative treatment for RCC, or various methods and their application, but instead explores in detail the anesthetic and physiologic considerations necessary once the decision to perform LPN has been made.

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Cardiovascular System

Physiologic Considerations

The most significant consideration for octogenarians undergoing LPN as opposed to any open procedure is the effect of pneumoperitoneum. The pressure necessary when insufflating carbon dioxide (CO_2) into the peritoneum for LPN is approximately 10 to 15 mm Hg. This increase in pressure has the potential to impact any collapsible structure, causing more distant pressure effects. The initial effect of pneumoperitoneum on the cardiovascular system is due to compression of the inferior vena cava, which causes an initial increase followed by sustained decrease in preload effect to the heart. This decrease in preload may then initiate a decrease in stroke volume (SV), and the overall effect on cardiac output (CO) depends on compensatory mechanisms, although studies have shown a decrease in CO of up to 30%.[15,16] To maintain end-organ perfusion, CO (in L/min) must be maintained to an individual degree, and as it is a product of SV and heart rate, compensation therefore takes place by an increase in one or both of these. Possible difficulties then arise in patients taking heart rate–controlling drugs such as β-blockers, which can prevent this compensatory increase.

Another consideration is systemic vascular resistance (SVR). An increase in SVR of between 25% and 35% has been documented in many studies, alongside an increase in pulmonary vascular resistance (PVR).[17] Potential mediators for this include catecholamines, prostaglandins, vasopressin, and the renin-angiotensin system.[18] During pneumoperitoneum, a rise in plasma adrenaline and noradrenalin is likely to cause the increase in SVR and mean arterial pressure. A rise in SVR causes an increase in afterload and a decrease in CO. The increase in SVR is, however, generally greater than the decrease in CO, therefore blood pressure is usually maintained or even increased. Conversely, at higher intra-abdominal pressures (IAPs), a significantly greater fall in CO is observed, with the inability to maintain blood pressure at these higher pressures. This effect is particularly pronounced in patients who are either hypovolaemic or have cardiovascular disease (CVD), and, therefore, careful control of IAP is necessary. The importance of euvolemia is therefore clearly demonstrated. There is, however, difficulty in the measurement of filling pressures as another effect associated with pneumoperitoneum, that of the cephalad shift of the diaphragm, which causes an increase in pleural pressure transmitted to the cardiac chambers. This can, therefore, give a falsely high central venous and mean pulmonary artery pressure.[18] A further component in the balance of CO/SVR is that of patient position, and it is well established that a head down position further exacerbates increase in SVR, whereas a head up position minimizes the increase seen.[19]

As heart rate increases alongside the increasing SVR and blood pressure, myocardial workload increases greatly. This leads us to the risk of myocardial ischemia. In patients with cardiac disease the back-pressure effects of an increase in SVR are augmented because of an increase in myocardial wall tension (ie, less compliance). It is more difficult to accommodate for lower filling pressures due to decreased venous return, coupled with increased afterload (ie, SVR, inability to increase SV, and tachycardia), and still maintain adequate CO. Also, length of diastole is decreased (when coronary artery; perfusion takes place), allowing for less filling time for the coronary arteries; hence, increasing the risk of myocardial ischemia. It is also clear from this rationale that those with coronary vessel disease will be further susceptible to these effects.

In the octogenarian, it is likely that a degree of coronary vessel disease and/or heart failure may be present, and it is known that, in the early stages of heart failure, there is activation of the sympathetic nervous system to provide inotropic support to the failing heart. Over time, prolonged activation causes downregulation of β_1 receptors and decreased ability of the myocardium to respond to sympathetic stimulation. Aging itself is also associated with increasing noradrenalin levels, further contributing to receptor downregulation.[20] Furthermore, should this hypothetical patient be taking a β-blocker, there is additional concern with regard to the efficacy of the sympathetic response, whereby blockade of β receptors would further reduce the heart's ability to respond to an adrenergic drive, and therefore further reduce myocardial reserve. The cause for this is the acute negative inotropic effects of the β-blocker in heart failure.[21]

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The hemodynamic effects of pneumoperitoneum are complex and patient dependant, with potential serious consequences in high-risk patients. This emphasizes the need for careful preoperative assessment prior to procedure planning. It is also necessary to use optimum intraoperative monitoring to carefully measure these parameters (eg, with a combination of arterial pressure and cardiac output via transesophageal Doppler echocardiography). There is limited evidence for the use of central venous pressure monitoring due to the false high readings obtained due to cephalad diaphragm shift, as previously mentioned. There is also some suggestion that preoperative intravascular preload can be effective in minimizing CO depletion.

Disease Prevalence and Preoperative Assessment

The current and widespread classification system for judging perioperative morbidity is the ASA score, which ranges from 1 to 6, and a recent large comparison of patients undergoing both laparoscopic and open PN found that 45% of all patients had an ASA score of at least 3.[22]

Careful CVD screening is important, with a necessity for careful examination and electrocardiographic monitoring for all elderly patients. A study by the British Geriatrics Society found that 75% of those > age 70 were receiving CVD medications, of which > 40% were for ischemic heart disease, and the majority for antihypertensive therapy.[23] The decision to pursue cardiovascular testing is only indicated if it is likely to alter perioperative management; however, it is not indicated in clinically stable patients. The American Heart Association recommends testing is only appropriate in those with functional limitation and ≥ 1 cardiac disease risk factor. First-line testing would be to perform dynamic stress tests with myocardial perfusion scanning, as stress testing may reveal those at risk of myocardial ischemia and infarction, and should stress testing be contraindicated, coronary angiography should be performed.[24] Should these indications occur, it would be advisable to refer the patient to a cardiologist prior to making any surgical decisions, as coronary angiography is not without risk.

The presence of atrial fibrillation (AF) can be particularly detrimental, as there is loss of atrial assistance with ventricular filling. Therefore, it may add to an already noncompliant myocardium when trying to maintain SV when venous return is decreased as a result of pneumoperitoneum. Diagnosis and optimization of AF is important preoperatively, with the expectation of intraoperative deteriorating cardiac function and planning for higher-level postoperative care. Other arrhythmias should also be considered and managed appropriately by a cardiologist prior to consideration of surgery; and notably those with second- and third-degree heart block will require either temporary or permanent pacemaker insertion prior to surgery.[25]

Following physical examination, should any cardiac murmur be detected, echocardiography should be performed, as degrees of aortic stenosis and regurgitation and mitral stenosis are common in this age group. General anesthesia in those with symptomatic or severe aortic stenosis is contraindicated and should be treated with aortic valve replacement prior to consideration of noncardiac surgery.[25]

Respiratory System

Physiology

Pneumoperitoneum has significant effects on mechanical ventilation. Insufflation of CO_2 into the peritoneum causes decreased diaphragmatic excursion, resulting in decreased functional residual capacity and lung compliance; it may also increase peak airway pressures, leading to possible CO_2 retention.[26] Some studies have shown a loss of functional residual capacity of up to 40%,[27] which could lead to ventilation-perfusion mismatch or intrapulmonary shunting and hypoxemia. Careful fine tuning of minute ventilation needs to take place with relatively large tidal volumes to avoid alveolar atelectasis and facilitate CO_2 clearance. It should be noted that, although the use of positive end-expiratory pressure significantly improves gas exchange, when intra-abdominal pressure is also high, there is a reduction in CO_2, and should be used with extreme caution.[28] Patients with chronic obstructive pulmonary disease (COPD) and emphysema are at increased risk of the detrimental effects of ventilation with pneumoperitoneum, coupled with the generalized effects of aging including decreased chest wall compliance and loss of elasticity of airways. Decreased lung compliance can lead to pulmonary barotraumas causing pneumothorax, although this has rarely been demonstrated in the literature.

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During pneumoperitoneum, it is generally accepted that a quantity of CO_2 will be absorbed systemically across the peritoneal membrane. In a young and healthy patient this will cause hypercarbia and acidemia, which can be easily reversed with changes in ventilation.[29] However, in those patients with pulmonary disorders, serious abnormalities in pH and pCO_2

may develop, leading to sequelae of mechanical and metabolic effects.[30] There is much emphasis on anesthetic experience in this group, as it can be clearly seen that balance is crucial in minimizing risk when ventilating these patients.

There should also be emphasis on quality of postoperative respiratory management, with awareness of the early signs of complications such as atelectasis, pneumonia, and hypoventilation, as these occur in a relatively high proportion of elderly patients. There appears to be no significant difference between the various means of respiratory dysfunction prophylaxis postoperatively, and various methods can be recommended at the discretion of the center, including conventional chest physiotherapy, incentive spirometry, and continuous positive airway pressure for those with higher risk of atelectasis and subsequent hypoxia, and lower respiratory tract infection.[31]

Another important consideration is postoperative pain management—inadequate pain control does not facilitate effective cough and clearance of respiratory secretions, and overuse of opiate analgesia combined with the residual effects of anesthetic agents and neuromuscular blockers can cause respiratory depression. This is considered one of the most common causes of death attributed to anesthesia,[32] and should be given special consideration in the elderly, as opiate requirement is generally lower than in younger patients,[33] and metabolism of medications can differ significantly, leading to potential increased pharmacologically active circulating medication quantities.

Disease Prevalence and Preoperative Assessment

It is difficult to estimate the prevalence of COPD in the general population, let alone the elderly, due to varying definitions and degrees of diagnosis; however, recent estimates using lung function testing measure prevalence as high as 13.3% in those over age 35 years.[34] Given the progressive nature of the disease, it is far more likely that significant and function-limiting disease will be present by age 80 years. There is evidence that preoperative optimization is effective in reducing complication rates in those with COPD with the use of mucolytic and bronchodilating agents.[35]

Spirometry is recommended in all patients who are either active or former smokers, and in any with known pulmonary disease of significant clinical symptoms, as increased residual volume and decreased forced expiratory volume in 1 second are good predictors of adverse outcome. Smoking within 1 month of elective surgery has been shown to increase intra- and postoperative risk sixfold; patients, on preassessment, should be advised to stop smoking at least 2 months prior to surgery to minimize increased risk of bronchospasm, mucus trapping, and regional atelectasis.[36]

Renal Considerations and Fluid Management

The elderly population has the fastest growth of end-stage renal disease, at 14% for those aged $\geq$ 75 years[37]; it appears that renal mass decreases progressively with age,[38] and loss of mass is mainly cortical, with general sparing of the medulla. As the kidney ages, there is also a decrease in the amount of both identifiable and intact glomeruli, and vascular adaptations occur to help reserve renal function via hyperperfusion and hyperfiltration. Renal arterial sclerosis also occurs, particularly alongside other comorbidities such as diabetes mellitus and hypertension, causing an overall decrease in renal blood flow of approximately 10% per decade in the past 40 years.[39] The effect of these changes is an estimated fall in glomerular filtration rate (GFR) of 8 mL/min/decade.[37] Pre- and postoperative estimate of GFR is essential for any renal surgery in the elderly, not only for estimation of loss of function, but for safe fluid administration and metabolism of drugs. Intraoperative IAP further contributes to decreased renal perfusion via decreased CO and increased SVR; without careful fluid balance and probable hyperfilling intraoperatively, this could lead to acute tubular necrosis. All patients should also be screened and treated for preoperative urinary tract infection to avoid any possible reversible renal compromise.

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Perioperative fluid management remains controversial and its optimization is key in maintaining organ perfusion and reducing the risk of peri- and postoperative complications. There are both cardiovascular and renal factors to take into account when managing fluids, and coupled with the difficulty in accurately measuring adequate filling (ie, falsely high central venous pressure measurements associated with pneumoperitoneum), balance may be difficult to achieve. There are also further difficulties—fluid overload cannot be identified accurately until its later and potentially catastrophic stages, nor can tissue perfusion (oxygen saturations and venous lactate give some data but there is no absolute measurement). Urine output must be monitored closely in order to accurately measure adequate hydration. It is globally recognized that 0.5 mL/kg/h is the minimum acceptable rate; however, at the discretion of the anesthetist, "overfilling" may be appropriate. In our institution, transesophageal cardiac output monitoring is also used.

The elderly are also more susceptible to fluid and electrolyte abnormalities, which are associated with increased morbidity and mortality during hospital stay. Their ability to both conserve and excrete sodium appropriately is compromised. In the context of intra- and postoperative fluid management, should sodium intake be reduced, they are unable to conserve it, predisposing them to hemodynamic instability and neurological complications associated with sodium loss.[40] They are also more prone to fluid volume expansion when challenged with sodium load, as excretion of sodium is impaired, predisposing them further to both pulmonary and peripheral edema, especially when coupled with cardiac disease. There is considerable risk in the administration of fluids in this group, as the risks of sodium depletion must be weighted against those of administering sodium in the form of intravenous crystalloid fluid.

Overall, the management of fluids in this group of patients should be left in expert hands, with careful preoperative assessment of hydration, and possible postoperative high-dependency unit placement for continual monitoring of both hydration status and serum urea and electrolytes in the early postoperative period.

Neurologic Considerations

Cerebrovascular Complications

Intraoperative hemodynamic instability is a well-recognized risk factor for ischemic stroke[41]; when combined with other likely risk factors in an elderly population (eg, physical inactivity, coexisting ischemic heart disease/cerebrovascular disease and hypertension), the risk of stroke is significant. Although risk does not necessarily alter intraoperative practice as hemodynamic instability is an independent problem, it should be included in postoperative management and awareness. The risk of postoperative ischemic stroke increases with age. One recent study estimated this to be 1% of noncardiac nonvascular procedures, and found that the most significant risk factors, aside from age, were previous stroke, renal disease, atrial fibrillation, and cardiac valvular disease.[42] Minimizing risk lies in preoperative assessment with careful examination for carotid bruits and general cardiological examination; all carotid bruits should be further assessed and treated at the discretion of a vascular surgeon.

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Postoperative Delerium and Cognitive Dysfunction

A disturbance in cognitive function both associated with hospital stay and postoperatively is common in the elderly, and can be transient and fluctuating in course (ie, delirium), or a more permanent change in neurological function (ie, postoperative cognitive dysfunction [POCD]). These changes have a significant impact on recovery, and length of hospital stay is estimated to increase fourfold.[43] During recovery, if cognitive dysfunction has declined, patients are at higher risk of accidents and injuries and are less able to follow specific postoperative instructions (eg, mobilization and nutrition).

The causes of delirium are often reversible, such as electrolyte disturbance, hypoxia, pain, and medications, and with careful investigation these causes can be removed. Causes of and risk factors for POCD are unclear despite several large, randomized control studies, but cerebrovascular disease, cerebral hypoperfusion, duration of anesthesia, and alteration in neurotransmitter function have all been suggested.[44] Despite anesthesia duration being a recognized risk factor, there is little evidence to suggest there is less risk with regional anesthesia compared with general anesthesia.[45] Incidence reporting varies and has been reported in 10% and 60% of elderly patients in the acute postoperative period, and as many as 25% of patients persisting with cognitive dysfunction after 3 months.[46]

Prevention of POCD is difficult due to unclear etiology, but should take the form of careful postoperative care with an awareness of medication effects and prevention of general postoperative complications. Its management should begin with preoperative assessment of cognitive function using an approved mental state examination so that any decline in function is easier to quantify. Further management will then depend on the detection of reversible causes, if present, and functional assessment and rehabilitation.

Venous Thromboembolism

The risk of venous thromboembolism (VTE) following surgery is well recognized, and preventative measures are in place worldwide. It should be of special consideration in this patient group due to other independent risk factors they possess: age (for those aged $<$ 40 years, annual incidence is 1/10,000 but this increases to 1/100 at age $>$ 80 years), malignancy, reduced mobility (a 10-fold increase with bed rest $>$ 3 days), and complex urological surgery (2- to 3-fold increase with general compared with regional anesthesia).[47] Other risks include duration of surgery, previous VTE, and both preexisting and new postoperative respiratory illness.

The Scottish Intercollegiate Guidelines Network has produced guidelines on prevention and management stating all patients admitted to the hospital should be individually assessed for risk of VTE and bleeding.[47] They advocate the use of antiembolism stockings in all patients unless contraindicated, with subcutaneous low molecular weight heparin, unfractionated heparin, or fondaparinux for those at moderate to high risk. The administration of anticoagulants should be used with caution after laparoscopic RN as there is moderate risk of bleeding, which is often subclinical until significant blood loss has taken place. In those who are deemed at significant risk of bleeding, intermittent pneumatic compression devices are recommended, but these should not take the place of anticoagulation once the bleeding risk is deemed reduced.

Drug Handling

Elderly patients tend to have increased adipose tissue, decreased muscle mass, and decreased total body water when compared with younger patients. When these factors are combined with decreased renal function, as well as subtle impairments in liver function, there can be significant impact in the way their body handles drugs. Pharmacokinetics are significantly affected by decreased total body water and increased adipose tissue, whereby there will be a decrease in volume distribution for those that are water-soluble and increase in volume distribution for those that are lipid-soluble. Therefore, hydrophilic drugs, due to smaller volume distribution, will have higher plasma concentration. Morphine, which can have as little as half the volume distribution compared with younger patients, has significantly amplified effects when given in the same dose to the elderly.[48]

Anesthetic agents tend to be protein-bound drugs, and albumin concentration in the elderly can be significantly reduced both in the healthy patient and more so in those undernourished. Free drug concentrations can be considerably higher, and propofol-free concentrations are especially affected as this drug is highly protein bound. The elderly brain is also more sensitive to propofol, and it is recommended that it be given far slower than in the young, with awareness of side effects.

Due to both decreased muscle mass and decreased muscle blood flow associated with aging, muscle relaxants can have amplified effects in the elderly, and when renal and hepatic excreted drugs are used, this can further amplify effects due to decreased clearance. Consideration of elimination means should take place during drug selection. It is often recommended that drugs cleared by Hoffman elimination and ester hydrolysis be chosen (eg, atracurium and cisatracurium).

Renal function should also be considered as GFR has been shown to decrease by around 8 mL/min/decade. All drugs undergo renal clearance at some stage, and water soluble metabolites will be excreted—of special note are certain muscle relaxants used during anesthetic and the opiate metabolite morphine-6-glucuronide, which depend on renal excretion. It is easy to accumulate this opiate metabolite in those with especially delayed excretion. The use of fentanyl is common postoperatively in patient-controlled analgesia (PCA) due to its fast action and short half-life. It has been shown that the dosage requirement in the elderly can be up to 50% less compared with younger-patient requirements,[49] and should be used with caution, especially in combination with benzodiazepines, due to their synergistic effects and risk of respiratory depression. Fentanyl is still the PCA drug of choice in our center for octogenarians postoperatively due to its short half-life and hepatic excretion when compared with morphine.

Conclusions

Age alone should not deter the use of LPN because, despite the challenges, outcomes in this patient group can be favorable, with unexpectedly low complication rates. The considerations prior to surgery planning are extensive and the decision to operate should encompass both surgical and anesthetic experience and viewpoints, as well as the choice of the informed patient. Careful preoperative assessment and planning should take place in order to minimize risk and optimize outcome. ■

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MAIN POINTS

- Laparoscopic partial nephrectomy (LPN) is now offered as an alternative for renal cell carcinoma in octogenarian patients. In addition to the well-established benefits of laparoscopic surgery, such as reduced postoperative pain, reduced hospital stay, and improved cosmetic appearance, other benefits may arise that are specific to the elderly.
- The most significant consideration for octogenarians undergoing LPN as opposed to any open procedure is the effect of pneumoperitoneum. The hemodynamic effects of pneumoperitoneum are complex and patient-dependant, with potential serious consequences in high-risk patients. This emphasizes the need for careful preoperative assessment prior to procedure planning.
- Prior to surgery, careful consideration and planning are key, and the decision to operate should include both surgical and anesthetic experience, as well as the choice of the informed patient. Careful preoperative assessment and planning should take place in order to minimize risk and optimize outcome.
- Age alone should not deter the use of LPN because, despite the challenges, outcomes in this patient group can be favorable with low complication rates.

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