REVIEW

OPEN

Preoperative laboratory testing in elderly patients

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Purpose of review
Preoperative testing in elderly patients is performed to examine the patient's current medical condition in the context of evaluating vulnerabilities and predicting postoperative complications to ensure that all functions recover before surgery. This review focused on preoperative laboratory tests in geriatric patients.

Recent findings
Preoperative complete blood count, electrolyte testing, and blood chemistry can predict postoperative complications. Preoperative elevated morning/evening salivary cortisol secretion ratio, C-reactive protein/albumin ratio (CAR), neutrophil/lymphocyte ratios, and preoperative decreased serum albumin level or 25-hydroxyvitamin D levels can predict postoperative cognitive dysfunction. Elevated brain-type natriuretic peptide or serum alkaline phosphatase levels can be biomarkers of major postoperative adverse cardiac events. Decreased preoperative estimated glomerular filtration rates and serum albumin levels can predict acute kidney injury. Hyponatremia, hypocalcemia, and low albumin/fibrinogen ratio predict postoperative complications. Hypoalbuminemia can predict surgical site infection or postoperative mortality after hip fracture surgery. A high CAR can predict anastomotic site leakage and is a risk factor for one-year mortality after hip surgery.

Summary
Preoperative laboratory testing helps predict postoperative adverse complications; thus, a plan of care can be initiated.

Keywords
aged, clinical laboratory tests, preoperative

INTRODUCTION

Preoperative evaluation of elderly (age 65 and older) patients is mostly performed by predicting the patient's functional reserve to minimize postoperative complications [1]. These assessments include a review of the characteristics of ordinary elderly patients, such as frailty, cognitive impairment, polypharmacy, nutrition, and limited capacity [2,3]. These assessments have limitations that should be comprehensively assessed by geriatric specialists. There are negative opinions as to whether a preoperative laboratory test is necessary solely because of old age as the test itself can harm elderly patients and lead to additional costs [4,5]. There are many reports that preoperative laboratory tests can be used as factors to predict postoperative complications. This review examined the possibility of predicting postoperative complications in currently used laboratory test results.

COGNITIVE ASSESSMENT

Preoperative cognitive impairment in the elderly is common, with an incidence of more than 20% among patients aged 65 years or older, with the highest prevalence among the oldest patients [6]. In-depth neuropsychiatric testing is impractical in most hospitals because many tests require training and are administered to individuals for over an hour. There is no universal cognitive testing tool that anyone can accept, regardless of anesthesia or patient condition. Having a biomarker that can detect

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Curr Opin Anesthesiol 2021, 34:409–414

DOI:10.1097/ACO.0000000000001008

KEY POINTS

- Recently, several preoperative laboratory tests, known as blood and chemistry tests, have been reported to predict common postoperative complications in elderly patients.
- Most of these tests are relatively inexpensive and less harmful to elderly patients.
- It allows immediate treatment for some test results that can be corrected, providing an opportunity to reduce postoperative morbidity and mortality in elderly patients.

cognitive impairment early will be valuable in preventing neurological side effects in elderly patients.

Cortisol is an essential primary stress hormone secreted by the adrenal glands in a 24-h cycle. Cortisol levels increase rapidly while awake and fall to their lowest levels around midnight. Causes of prolonged high glucocorticoid levels include abnormal circadian rhythms, aging, trauma, depression, and neurodegenerative diseases. Han *et al.* collected saliva samples from 120 (>60 years) elderly patients twice a day from 6:00 to 7:30 a.m. and from 9:30 to 11:00 p.m. before surgery. They observed postoperative cognitive dysfunction (POCD) in 17.02% of patients after surgery and reported that a higher preoperative 6:00 to 7:30 a.m.(AM) / 9:30 to 11:00 p.m.(PM) salivary cortisol ratio (POCD vs. non-POCD: 5.16 vs. 2.60; $P = 0.006$) predicted early POCD (odds ratio [OR] 1.56, 95% confidence interval [CI] 1.20–2.02; $P = 0.001$) [7▪▪].

The concentration of albumin decreases with aging, hepatic disease, malnutrition, and expansion of the plasma volume status, which responds to surgical stimuli [8]. A retrospective study by Qi *et al.* was conducted on 328 elderly patients that investigated the possibility of predicting changes in the rate of albumin on the day before and the second day after surgery for postoperative delirium (POD). After total joint arthroplasty, POD was observed in 20.7% of patients, and the relative change in albumin value (POD vs. non-POD: $18.8 \pm 3.7\%$ vs. $13.6 \pm 3.3\%$, $P < 0.001$) predicted POD (OR 2.43, 95% CI 1.17–4.86; $P = 0.015$) [9]. According to another study on the ratio of C-reactive protein and albumin ratio (CAR) by Peng *et al.* in 272 elderly patients (aged 65–85 years) following total joint arthroplasty, POD was observed in 20.2% of patients, and a high preoperative CAR (2.9 ± 0.8) may be a predictor for POD (OR 3.04, 95% CI 1.23–7.23; $P = 0.016$; cut-off value: 2.35) [10].

A few studies have reported that low vitamin D concentrations are associated with an increased risk of cognitive decline [11]. However, those with a longer follow-up observation did not show the same results. Recently, Gao *et al.* investigated 257 elderly patients to assess the risk factors for POCD. They observed POCD in 21.4% of patients; their preoperative 25-hydroxyvitamin D serum level (POCD vs. non-POCD: 12.2 ± 4.7 ng/mL vs. 15.4 ± 5.8 ng/mL, $P = 0.001$) was a risk factor for POCD (OR: 1.77, 95% CI 1.13–2.78; $P = 0.016$) after total joint arthroplasty [12].

Neutrophil and lymphocyte counts are widely used as inflammatory biomarkers of systemic inflammation. The ratio of neutrophils to lymphocytes was readily calculated from blood examination. Yong *et al.* reported that POCD was observed in 19% of 221 elderly patients (≥65 years), and preoperative neutrophil-lymphocyte ratio (NLR) (cut-off value, ≥2.50) was a risk factor for POCD (OR 2.44, 95% CI 1.52–3.68; $P = 0.013$) [13]. Moreover, NLR can be readily obtained from the results of a standard complete blood examination. Based on their study, cognitive monitoring and progressive intervention are required for elderly patients with a high NLR. Table 1 summarizes the predictability of preoperative variables to predict POCD or POD.

Table 1. Logistic regression analysis of variables predicting postoperative cognitive complication

	Age	Sample size	POCD vs. Non-POCD	OR [95% CI]
AM/PM salivary cortisol ratio [7▪▪]	>60	120	5.16 vs. 2.60	1.56 [1.20–2.02]
25-hydroxyvitamin D serum (ng/mL) [12]	≥65	257	12.2 vs. 15.4	1.77 [1.13–2.78]
Neutrophil-lymphocyte ratio [13]	≥65	221	2.71 vs. 2.38	2.44 [1.52–3.68]
			POD vs. Non-POD	
Relative change in albumin value [9]	≥65	328	18.8 vs. 13.6	2.43 [1.17–4.86]
CAR [10]	>65	272	2.9 vs. 2.1	3.04 [1.23–7.23]

CAR, C-reactive protein-to-albumin ratio; CI, confidence interval; OR, odds ratio; POCD, postoperative cognitive dysfunction; POD, postoperative delirium. Relative change in albumin value is defined as the absolute value of (preoperative albumin value − nadir value within postoperative day 2)/preoperative albumin × 100%.

Table 2. Logistic regression analysis of variables predicting postoperative cardiac complication

	Age	Sample size	OR [95% CI]	Complication
NT-pro BNP [16▪]	>45	9,789		POAF
200 ng/L			1.31 [1.15–1.49]	
1500 ng/L			2.07 [1.27–3.36]	
3000 ng/L			2.39 [1.26–4.51]	
Elevated serum ALP (>79 IU/L) [17]	>65	1,395	4.507 [1.37–14.73]	cardiac and cerebrovascular events
			HR [95% CI]	
Low serum ALT (≤13 IU/L) and High AST/ALT ratio (>1.62) [22]	62[52–70]	6,264	1.58 [1.14–2.18] 1.59 [1.15–2.20]	mortality after cardiovascular surgery

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; HR, hazard ratio; NT-pro BNP, N-terminal pro-brain-type natriuretic peptide; OR, odds ratio; POAF, postoperative atrial fibrillation.

These studies suggest that these biomarkers may be useful for screening vulnerable patients with POCD, and some of them are considered modifiable risk factors for postoperative complications. Regardless of the preoperative examination, if the cognitive abilities of elderly patients can be predicted before surgery, proper perioperative care can be taken immediately to reduce POCD. This surgical prevention of postoperative complications is very important because central nervous system complications are not only a major cause of morbidity and mortality but can also negatively affect the patient's quality of life, family, and medical costs.

CARDIOVASCULAR SYSTEM

Cardiovascular complications are associated with the greatest perioperative mortality in geriatric patients, in part from age-related comorbid diseases and in part from the reduction in organ reserve. In the absence of arrhythmia, aging of the cardiac conduction and autonomic systems leads to decreased heart rate variability and an increased incidence of ectopic beats [14]. Arrhythmia can decrease cardiac output in older adults. The prevalence of atrial fibrillation increases with age, affecting 1 in 10 patients aged ≥80 years [15].

Circulating brain-type natriuretic peptide (BNP) is a biomarker of cardiovascular outcomes, produced mainly in ventricular cardiomyocytes under volume or pressure overload stimuli. Szczeklik *et al.* conducted a prospective study to investigate the predictive value of N-terminal pro-BNP (NT-proBNP). The incidence of postoperative atrial fibrillation (POAF) was 1.0% in 37,664 patients (aged ≥45 years) without atrial fibrillation, and they reported the incidence of POAF to be 1.0%. Preoperative NT-proBNP levels have been shown to predict POAF. Compared with a reference value of 100 ng/L, preoperative NT-proBNP levels of 200, 1500, and 3000 ng/L are related to adjusted ORs for POAF of 1.31 (95% CI 1.15–1.49), 2.07 (1.27–3.36), and 2.39 (1.26–4.51), respectively [16▪]. In their study, they also showed that age >65 years and >80 years were related to ORs for POAF of 2.06 (95% CI 0.92–4.61) and 4.37 (1.91–9.98).

Many factors are related to vascular calcification. Inorganic pyrophosphate acts as a potent inhibitor of growth and tissue calcification. Alkaline phosphatase (ALP) promotes cardiovascular calcification by reducing pyrophosphate levels. You *et al.* retrospectively analyzed 1,395 elderly patients undergoing spinal surgery. Elevated serum ALP (>79 IU/L) predicted major adverse cardiac and cerebrovascular events (OR 4.507, 95% CI 1.378–14.739; $P = 0.013$). Preoperative serum ALP levels may be a predictive biomarker of 30-day postoperative cardiovascular and cerebrovascular adverse events following spinal fusion [17]. Table 2 summarizes the predictable ability of preoperative variables to predict postoperative cardiovascular complications.

These studies suggest that these biomarkers may be useful for aged hearts. Aging alterations make their heart and vascular systems more sensitive to anesthesia or vascular volume changes, thus limiting their ability to respond to unstable hemodynamic changes during surgery. Therefore, a clear understanding of the functional limitations of the cardiovascular system will enable effective perioperative management.

RENAL FUNCTION TEST

After 50 years of age, the average kidney weight decreases from approximately 250 g to 180 g, mostly due to cortical atrophy from glomerulosclerosis. Additionally, the glomerular filtration rate (GFR) decreases to approximately 80 mL/min/m^2 at age 60 and 60 mL/min/m^2 at age 80 [18]. Acute kidney

injury (AKI) is a common and serious complication. Elderly patients are at a higher risk of developing AKI because of a lack of functional reserve.

According to a recent retrospective cohort study of 668 very elderly (≥80 years) patients, the estimated GFR before surgery, calculated based on the Modification of Diet in the Renal Disease Study equation, is a risk factor for postoperative AKI (OR 2.662, 95% CI 1.264–5.608; $P = 0.01$). The incidence of postoperative AKI is significantly higher among patients with lower preoperative estimated GFR than among those with estimated GFR ≥70 mL/min/1.73 m^2 ($P = 0.003$) [19]. Although their work has many limitations in interpretation (such as neglecting various surgical burdens), late postoperative factors, AKI duration, and preoperative estimated GFR can help evaluate postoperative AKI.

Elderly patients with hip fractures are associated with a high mortality rate. The prevalence of malnutrition in these patients varies significantly. Among preoperative laboratory values, low albumin is a predictor of increased length of hospital stay and the possibility of postoperative complications. Particularly, preoperative hypoalbuminemia affected AKI development at preoperative albumin levels of 2.9 ± 0.4 g/dL as well as postoperative albumin levels of 2.4 ± 0.3 g/dL in elderly patients (≥65 years) following hip fracture surgery [20].

The mechanism is not yet known, but it can be seen that if elderly patients have acute injury, illness, or chronic difficulty in eating and drinking, the homeostasis of body fluids, electrolytes, and protein metabolism becomes vulnerable.

LIVER FUNCTION TEST

There is a reduction in liver size by the age of 60, probably due to the decrease in hepatic and splanchnic blood flow of 40% [21]. There were no age-specific alterations in the routine liver function tests. Hepatocellular injury increases serum levels of aspartate aminotransferase (AST; serum glutamic oxaloacetic transaminase) and alanine aminotransferase (ALT; serum glutamic pyruvic transaminase).

A recent observational cohort study of 6,264 adults (median age, 62 years; interquartile range, 52–70 years) undergoing cardiovascular surgery showed that a low preoperative ALT level (≤20th percentile, ≤13 IU/L) and high AST/ALT ratio (>80th percentile, >1.62) were associated with increased postoperative mortality. ALT levels are relatively specific to hepatic aging, liver volume, and functional liver cells, since low ALT levels are more strongly associated with the risk of death. They suggest that preoperative serum aminotransferase levels can be a prognostic biomarker for elderly patients after cardiovascular surgery [22]. Although their study design is not limited to elderly patients and has limitations in the generalization of their transaminase levels, it is meaningful that the level of aminotransferase that is usually tested for identifying liver function can be used to predict postoperative mortality after cardiovascular surgery.

COMPLETE BLOOD COUNT

The preoperative hemoglobin value has been proposed as a necessary test for many patients prior to elective surgery, but even the need for a test that meets this minimum standard is still being questioned.

In the case of appendicitis in elderly patients, even though it is an acute inflammatory disease that causes abdominal pain, the symptoms and physical examinations are not clear, and the inflammatory response (staphylococcal action, cytokine pool) can be blunted. These features can delay diagnosis and increase complications, such as perforation and peritonitis. Bayrak *et al.* retrospectively examined 4,121 patients who underwent open or laparoscopic appendectomy and reported that the white blood cell (WBC) count, lymphocyte count, and neutrophil/WBC ratio of in elderly patients were higher than those in younger patients ($P < 0.001$, $P = 0.013$, and $P = 0.021$, respectively). WBC values >12.11 × 10^3/μL may predict acute appendicitis in elderly patients (age ≥65 years) [23].

ELECTROLYTES

Approximately 2.5% of hospitalized patients show hyponatremia, which is 10 times more common in elderly patients. Diuretic-induced renal dysfunction; age-related high secretion of antidiuretic hormone; impaired function to excrete free water; decreased dietary intake; and increased loss from vomiting, diarrhea, and chronic blood loss contribute to hyponatremia in elderly patients. A recent retrospective study of 842 patients who underwent radical gastrectomy demonstrated that preoperative hyponatremia (<135 mEq/L, $P = 0.001$) and hypocalcemia (calcium < 8.0 mg/dL or < 2.0 mmol/L; ionized calcium < 1.0 mmol/L, $P = 0.038$) predicted postoperative adverse effects and overall survival in elderly gastric cancer patients (≥60 years). Hypocalcemia was associated with shorter overall survival in elderly patients (hazard ratio 0.674, $P = 0.037$) [24]. Hyponatremia or hypocalcemia may affect the function of the central nervous system or cardiovascular system and are associated with significant postoperative morbidity and mortality. Hyponatremia or hypocalcemia in elderly patients should be

Table 3. Logistic regression analysis of variables predicting postoperative complication

	Age	Sample size	OR [95% CI]	Complication
Low AFR (<7.4) [25]	≥65	365	1.94 [1.09–3.36]	Severe postoperative complications
Low serum albumin (<2.9g/dL) [26▪]	≥65	1,083	1.6 [1.2–2.4]	Early mortality after hip fracture surgery
<3.5g/dL [27]	≥65	611	2.76 [1.17–4.31]	Surgical site infection
High CAR (>3.3) [28]	≥65	1,068	1.94 [1.21–3.11]	Anastomotic leakage
>2.49 [29]	≥65	254	3.52 [1.49–8.3]	1 year mortality after hip fracture surgery
>1.47 [30]	>60	224		Post-THA contralateral hip refracture

AFR, albumin-to-fibrinogen ratio; CAR, C-reactive protein-to-albumin ratio; CI, confidence interval; OR, odds ratio; THA, total hip arthroplasty.

corrected as soon as possible to prevent postoperative complications.

PROTEIN AND BLOOD CHEMISTRY

Albumin, as a sensitive nutritional biomarker, decreases after surgery due to surgical stress and increased capillary leakage. Fibrinogen, which is synthesized by the liver, is an essential protein for the coagulation cascade as well as an acute-phase reaction protein produced in response to systemic inflammation. Low preoperative fibrinogen has been suggested as a potential risk factor for neurological complications. The albumin/fibrinogen ratio (AFR) combines these two biomarkers and amplifies the sensitivity of the evaluation of inflammatory and nutritional status. You *et al.* conducted a retrospective study of 365 elderly patients with gastric cancer (≥65 years) who underwent radical laparoscopic gastrectomy. They found that 14.2% of the patients developed postoperative complications within 30 days, and preoperative low AFR (7.4 ± 2.1; cut-off value, 8.49) was a predictor of postoperative complications (OR 1.94, 95% CI 1.09–3.36, $P = 0.017$) [25].

Lizaur-Utrilla *et al.* showed that preoperative altered serum albumin (<2.9 g/dL; OR, 1.6; 95% CI, 1.2–2.4; $P = 0.013$), sodium (<127 mEq/L; 1.4 [95% CI 1.1–2.4]; $P = 0.035$), and parathyroid hormone levels (>65 pg/mL; 1.3 [95% CI 1.0–3.4]; $P = 0.005$) were predictors of 30-day postoperative early mortality (8.2%) following hip fracture surgery in a prospective study of 1,083 elderly patients (≥65 years) [26▪].

Surgical site infection following hip fractures is an important postoperative complication, with an incidence rate of 1.3–16.9%. A recent retrospective study of 611 elderly patients (≥65 years) to assess modifiable factors for reducing surgical site infection following hip fracture surgery was conducted by Ma *et al.*, who suggested that current smoking, preoperative hypoalbuminemia (<3.5 g/dL), and elevated fasting blood sugar (>110 mg/dL) should be optimized preoperatively to reduce infections [27].

C-reactive protein (CRP) and albumin are two circulating acute-phase proteins that respond to inflammation. CRP is closely related to trauma, inflammation, and bacterial infection. Yu *et al.* showed a relationship between an active systemic inflammatory response and anastomotic leakage after colorectal surgery. Among 1,068 elderly patients (≥65 years), 7.6% developed anastomotic leakage; a preoperative high CAR (3.3 ± 1.1) was a predictor of anastomotic leakage (OR 1.94, 95% CI 1.21–3.11; $P = 0.007$) [28]. Another retrospective study of 254 elderly patients to investigate the relationship between preoperative CAR and 1-year mortality after hemiarthroplasty due to hip fracture showed that the 1-year mortality rate was 22.8%; a preoperative CAR > 2.49 was an indicator of 1-year mortality (OR 3.52, 95% CI 1.49–8.3; $P = 0.004$) [29]. Chen *et al.*'s study of 224 elderly patients (>60 years) with postsurgery contralateral hip fracture also showed that a preoperative elevated CAR (1.47 ± 0.27, $P < 0.001$, optimal cut-off: 1.12) was a risk factor for contralateral hip fracture post-total hip arthroplasty [30]. Table 3 summarizes the predictability of preoperative blood chemistry variables to predict postoperative surgical complications.

According to the literature, laboratory test results provide valuable information regarding predictions of postoperative adverse effects. Although albumin levels are insufficient to measure incomplete nutritional status and the clinical usefulness of CRP is limited, they are relatively inexpensive tests and can predict various postoperative complications.

CONCLUSION

Recently published literature has shown that there is a limit to the interpretation of various laboratory test results regarding the prediction of postoperative

complications, but preoperative laboratory tests can predict postoperative adverse effects. This provides a realistic opportunity to establish optimal geriatric patient-centered care plans.

Little is known about the mechanisms underlying various postoperative complications in geriatric patients. Since elderly patients have complex preoperative situations, postoperative complications are often multifactorial and there is no single 'magic bullet' to solve them. Our understanding of preoperative laboratory testing has evolved in recent years. It is highly recommended to conduct appropriate laboratory tests because these laboratory test results can lead to improved results. Beyond this, additional multidisciplinary efforts are needed to establish optimal testing, cost efficiency, and safety profiles for elderly patients.

Acknowledgements

We would like to thank professor Seok-Kyeong Oh for his contribution to find references.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

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