Preoperative laboratory testing in elderly patients

Kyung-Cheon Lee and Il-Ok Lee

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...
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; their preoperative 6:00 to 7:30 a.m./9:30 to 11:00 p.m. saliva cortisol ratio (POCD vs. non-POCD: 2.9 ± 0.8; P = 0.015) was a risk factor for POD (OR 3.04, 95% CI 1.13–7.23; 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 POD (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

| Variable                                      | Age | Sample size | P OCD 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] |
| 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] |

POD vs. Non-POD

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.
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/m² at age 60 and 60 mL/min/m² 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 m² (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 splanchinic 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 × 10^9/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
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 response and anastomotic leakage; a preoperative high AFR (3.3\(\times\)1.1) was a predictor of postoperative complications (OR 1.94, 95\% CI 1.21–3.11; \(P=0.007\)) [28]. Another retrospective study of 254 elderly patients (\(>60\) years) with postsurgery contralateral hip fracture surgery also showed that a preoperative elevated AFR (2.49) was an indicator of 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 post-surgery contralateral hip fracture also showed that a preoperative elevated CAR (1.47 \(\times\)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 bone 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.

**Table 3.** Logistic regression analysis of variables predicting postoperative complication

| Variable | Age | Sample size | OR [95\% CI] | Complication |
|----------|-----|-------------|--------------|--------------|
| Low AFR (<7.4) [25] | \(\geq 65\) | 365 | 1.94 [1.09–3.36] | Severe postoperative complications |
| Low serum albumin (<2.9 g/dL) [26*] | \(\geq 65\) | 1,083 | 1.6 [1.2–2.4] | Early mortality after hip fracture surgery |
| <3.5 g/dL [27] | \(\geq 65\) | 611 | 2.76 [1.17–4.31] | Surgical site infection |
| High CAR (>3.3) [28] | \(\geq 65\) | 1,068 | 1.94 [1.21–3.11] | Anastomotic leakage |
| >2.49 [29] | \(\geq 65\) | 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.

Preoperative laboratory testing in geriatrics: Lee and Lee

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 (\(\geq 65\) years), 7.6\% developed anastomotic leakage; a preoperative high CAR (3.3\(\times\)1.1) was a predictor of anastomotic leakage (OR 1.94, 95\% CI 1.21–3.11; \(P=0.007\)) [28].
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-Kyong Oh for his contribution to find references.

Financial support and sponsorship
None.

Conflicts of interest
There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

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

* of special interest
** of outstanding interest

1. Silverstein JH. The practice of geriatric anesthesia. In: Silverstein JH, Alec Rooste G, Reves JG, et al. editors. Geriatric anesthesiology. New York, USA: Springer Science + Business Media LLC; 2008. pp. 3–14.
2. Oresanya LB, Lyons WP, Finlayson E. Preoperative assessment of the older patient: a narrative review. JAMA 2014; 311:2110–2120.
3. Lim BG, Lee IO. Anesthetic management of geriatric patients. Korean J Anesthesiol 2020; 73:8–29.
4. Chen CL, Lin GA, Bardach NS, et al. Preoperative medical testing in Medicare patients undergoing cataract surgery. N Engl J Med 2015; 372:1520–1528.
5. Kirkham KR, Wijeyasurya DN, Pindrith C, et al. Preoperative laboratory investigations: rates and variability prior to low-risk surgical procedures. Anesthesiology 2016; 124:804–814.
6. Culley DJ, Flaherty D, Reddy S, et al. Preoperative cognitive stratification of older elective surgical patients: a cross-sectional study. Anesth Analg 2016; 123:186–192.
7. Han Y, Han L, Dong MM, et al. Preoperative salivary cortisol AM/PM ratio predicts early postoperative cognitive dysfunction after noncardiac surgery in elderly patients. Anesth Analg 2019; 128:349–357.
8. Han Y, Wang H, et al. Preoperative C-reactive protein/albumin ratio, a predictor of cardiac and cerebrovascular complications after lumbar spinal fusion surgery in elderly: a retrospective study. J Clin Med 2019; 8:1111, 11 pages.
9. Aalami OO, Fang TD, Song HM, et al. Physiological features of aging persons. Curr Pharm Sci 2009; 11:1068–1076.
10. Wu Q, Yang H, Bo H, et al. Predictive role of estimated glomerular filtration rate prior to surgery in postsurgical acute kidney injury among very elderly patients: a retrospective cohort study. Ren Fail 2019; 41:866–874.
11. Kupeli T, Unver S, The correlation between preoperative and postoperative hypoaluminemia and the development of acute kidney injury with respect to the KDIGO criteria in the hip fracture surgery in elderly patients. Turk J Anaesthesiol Reanim 2020; 48:38–43.
12. Rivera R, Antognini JF. Perioperative drug therapy in elderly patients. Anesthesiology 2009; 110:1176–1181.
13. Nam JS, Kim WJ, An SM, et al. Age-dependent relationship between preoperative serum aminotransferase and mortality after cardiovascular surgery. Aging 2019; 11:9006–9074.
14. Baynak S, Tatar C, Caker E, et al. Evaluation of the predictive power of laboratory markers in the diagnosis of acute appendicitis in the elderly. North Clin Istanbul 2019; 6:293–301.
15. Xu J, Chen X, Wang X, et al. Preoperative hyponatremia and hypocalcemia predict poor prognosis in elderly gastric cancer patients. Cancer Manag Res 2020; 12:8799–8807.
16. You X, Zhou Q, Song J, et al. Preoperative albumin-to-fibrinogen ratio predicts severe postoperative complications in elderly gastric cancer subjects after radical laparoscopic gastrectomy. BMC Cancer 2019; 19:931, 8 pages.
17. Lizarz-Urilla A, Gonzalez-Navarro B, Vizcaya- Moreno MF, et al. Altered serum levels of albumin, sodium and parathyroid hormone may predict early mortality following hip fracture surgery in elderly. Int Orthop 2019; 43:2825–2829.
18. Ma T, Lu K, Song L, et al. Modifiable factors as current smoking, hypobulinemia, and elevated fasting blood glucose level increased the SSI risk following elderly hip fracture surgery. J Investig Surg 2020; 33:750–758.
19. Yu Y, Wu Z, Shen Z, et al. Preoperative C-reactive protein-to-albumin ratio predicts anastomotic leak in elderly patients after curative colorectal surgery. Cancer Biomark 2020; 27:295–302.
20. Capkin S, Guler S, Ozmenvera R. C-reactive protein to albumin ratio may predict mortality for elderly population who undergo hemiarthroplasty due to hip fracture. J Investig Surg 2020; 16:1–6.
21. Chen L, Zhang J, Zhang W, et al. Correlation between C-reactive protein/albumin and contralateral hip fracture after total hip arthroplasty in elderly patients with hip fractures. Ann Palliat Med 2020; 9:1055–1061.