Machine learning-based prediction of off-pump coronary artery bypass grafting-associated acute kidney injury

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Background: The cardiac surgery-associated acute kidney injury (CSA-AKI) occurs in up to 1 out of 3 patients. Off-pump coronary artery bypass grafting (OPCABG) is one of the major cardiac surgeries leading to CSA-AKI. Early identification and timely intervention are of clinical significance for CSA-AKI. In this study, we aimed to establish a prediction model of off-pump coronary artery bypass grafting-associated acute kidney injury (OPCABG-AKI) after surgery based on machine learning methods.

Methods: The preoperative and intraoperative data of 1,041 patients who underwent OPCABG in Chest Hospital, Tianjin University from June 1, 2021 to April 30, 2023 were retrospectively collected. The definition of OPCABG-AKI was based on the 2012 Kidney Disease Improving Global Outcomes (KDIGO) criteria. The baseline data and intraoperative time series data were included in the dataset, which were preprocessed separately. A total of eight machine learning models were constructed based on the baseline data: logistic regression (LR), gradient-boosting decision tree (GBDT), eXtreme gradient boosting (XGBoost), adaptive boosting (AdaBoost), random forest (RF), support vector machine (SVM), k-nearest neighbor (KNN), and decision tree (DT). The intraoperative time series data were extracted using a long short-term memory (LSTM) deep learning model. The baseline data and intraoperative features were then integrated through transfer learning and fused into each of the eight machine learning models for training. Based on the calculation of accuracy and area under the curve (AUC) of the prediction model, the best model was selected to establish the final OPCABG-AKI risk prediction model. The importance of features was calculated and ranked by DT model, to identify the main risk factors.

Results: Among 701 patients included in the study, 73 patients (10.4%) developed OPCABG-AKI. The GBDT model was shown to have the best predictions, both based on baseline data only (AUC =0.739, accuracy: 0.943) as well as based on baseline and intraoperative datasets (AUC =0.861, accuracy: 0.936). The ranking of importance of features of the GBDT model showed that use of insulin aspart was the most important predictor of OPCABG-AKI, followed by use of acarbose, spironolactone, alfentanil, dezocine, levosimendan, clindamycin, history of myocardial infarction, and gender.

Conclusions: A GBDT-based model showed excellent performance for the prediction of OPCABG-AKI. The fusion of preoperative and intraoperative data can improve the accuracy of predicting OPCABG-AKI.

Introduction

Acute kidney injury (AKI) is a serious complication after cardiac surgery (1). A meta-analysis (2) reported that the incidence of cardiac surgery-associated acute kidney injury (CSA-AKI) was approximately 26.0–28.5%. The 28- and 90-day mortality rate of patients with CSA-AKI have been shown to reach 10.7% and 30%, respectively (3). The pathogenesis of CSA-AKI is complex and includes ischemia-reperfusion injury, inflammation from surgical trauma, oxidation, and other factors (4,5). Although off-pump coronary artery bypass grafting (OPCABG) can avoid ischemia-reperfusion injury (6), the hemodynamic impact of the procedure and the possible incomplete revascularization can still increase the risk of off-pump coronary artery bypass grafting-associated acute kidney injury (OPCABG-AKI) (7-9). Therefore, it is of great clinical significance to establish an accurate prediction model for OPCABG-AKI to identify the high-risk patients (10,11). Recently, CSA-AKI has been predicted by machine learning in many studies (12-15). However, these studies included a large number of surgical types, inconsistent definitions of AKI and incorporated few intraoperative data (16). In this study, we compared the performance of eight different machine learning models to predict OPCABG-AKI, in order to select the optimal model for identifying high-risk patients early and guiding perioperative clinical decision-making. We present this article in accordance with the TRIPOD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-711/rc).

Methods

Study population

The preoperative and intraoperative data of 1,041 patients who underwent OPCABG in Chest Hospital, Tianjin University from June 1, 2021 to April 30, 2023 were collected. The average age of these patients was 67.69±6.59 years, and the number of males and females was 743 and 298, respectively. After screening and excluding patients with missing data, the data of 701 patients were finally included in the dataset. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Medical Ethics Committee of Chest Hospital, Tianjin University (No. 2021 KY-008-01). The requirement for informed consent was waived due to the retrospective nature of this study. The confidentiality and privacy of patients was guaranteed.

OPCABG-AKI diagnostic criteria

The definition of AKI was based on the serum creatinine (SCr) based Kidney Disease Improving Global Outcomes (KDIGO) criteria (17). However, the urine output criteria were not used due to lack of data. The diagnostic criteria were therefore as follows: SCr rises by ≥26.5 µmol/L (≥0.3 mg/dL) or SCr rises to ≥1.5 times compared to baseline within 7 days after surgery; or need for renal replacement therapy.

Highlight box

Key findings
- The gradient-boosting decision tree model was deemed the best model for predicting off-pump coronary artery bypass grafting (OPCABG)-associated acute kidney injury (AKI) (OPCABG-AKI) out of a set of eight machine learning models. The addition of intraoperative time series data in addition to baseline data may improve predictive performance.

What is known and what is new?
- OPCABG is one of the major cardiac operations leading to cardiac surgery associated-acute kidney injury (CSA-AKI). Early recognition and timely intervention have important clinical significance for CSA-AKI.
- This study aimed to establish a prediction model of OPCABG-AKI through machine learning method.

What is the implication, and what should change now?
- Early recognition and timely intervention have important clinical significance for OPCABG-AKI.

Data collection and data preprocessing

The training set comprised 80% of the dataset and the test set comprised the remaining 20% of the dataset, including baseline data and intraoperative time series data. The baseline data included the preoperative data, intraoperative variables, and discrete variable data. The indicators with a missing rate over 10% were deleted, and then the remaining values were processed. Intraoperative time series data were collected by LiDCO hemodynamic monitor (Masimo, Irvine, CA, USA), Nonin oximeter (Nonin Medical, Plymouth, MN, USA), Philips multi-parameter portable ECG monitor (Philips, Amsterdam, The Netherlands), and Ohmeda anesthesia machine (GE Healthcare, Chicago, IL, USA), and the sampling frequency was adjusted to 1 Hz. Variables with the same value were considered as outliers, and indicators with an outlier rate of more than 10% were removed, and then missing numerical variables were imputed by the upper and lower means, and modal imputation was used for categorical variables.

Predictors

The predictors used for machine learning model development were detailed in Table S1.

Statistical analysis

A total of eight machine learning models were trained to predict OPCABG-AKI based on the baseline data only, including logistic regression (LR), support vector machine (SVM), decision tree (DT), random forest (RF), k-nearest neighbor (KNN), gradient-boosting decision tree (GBDT), adaptive boosting (AdaBoost), and eXtreme gradient boosting (XGBoost). In this study, k-fold cross-validation was adopted, and k was set to 10, that is, the original data was randomly divided into 10 parts without repeated sampling. One of them is selected as the test set at a time, and the remaining nine are used as the training set to train the model. Repeat step 2 10 times to get a model after training on each training set. Test the model against the appropriate test set, calculate and save the model's evaluation metrics. The average of the 10 groups of test results is calculated as an estimate of the accuracy of the model and as a performance index of the model under the current k-fold cross-validation. The intraoperative time series data were extracted by means of a long short-term

memory (LSTM) deep learning model. The baseline data and the extracted intraoperative features were fused by the transfer learning and fed into each of the eight machine learning models for further training. The model with the best predictive performance was identified based on the calculated accuracy and area under the curve (AUC). Afterwards, the feature importance was calculated and ranked by DT model to screen out the main risk factors. All statistical analyses were performed using SPSS version 26. The statistical analysis plan was depicted in *Figure 1*.

Results

Prediction of OPCABG-AKI by machine learning methods

Among 701 patients included in the study, 73 (10.4%) developed OPCABG-AKI. The patients inclusion flowchart was showed in *Figure 2*. *Table 1* shows the performance of the models based on the baseline data only; the AUC of the GBDT model was the highest (AUC =0.739), followed by AdaBoost model (AUC =0.732), SVM model (AUC =0.731), LR model (AUC =0.717), XGBoost model (AUC =0.698), RF model (AUC =0.647), KNN model (AUC =0.578), and DT model (AUC =0.517). *Table 2* shows the performance of these models when intraoperative data were added to the baseline data; the AUC of the GBDT model was again the highest (AUC =0.861), followed by RF model (AUC =0.780), XGBoost model (AUC =0.764), SVM model (AUC =0.730), AdaBoost model (AUC =0.726), LR model (AUC =0.700), KNN model (AUC =0.598) and DT model (AUC =0.550). These data demonstrate that the addition of intraoperative time series data resulted in a considerable increase in AUC; in case of the GBDT model, AUC increased by 0.122.

Interpretability of machine learning models in AKI forecasting

The top 20 features of the GBDT model for feature importance are shown in *Figure 3*. Use of insulin aspart is the most important feature of OPCABG-AKI, followed by use of acarbose, spironolactone, alfentanil, dezocine, levosimendan, clindamycin, history of myocardial infarction, sex, cerebral tissue oxygen saturation (SctO$_2$; left), SctO$_2$ (right), lactate, creatine kinase (CK), troponin, heart rate, family history of surgery, clopidogrel, age, systemic vascular resistance (SVR), and angiotensin receptor blockers (ARBs).
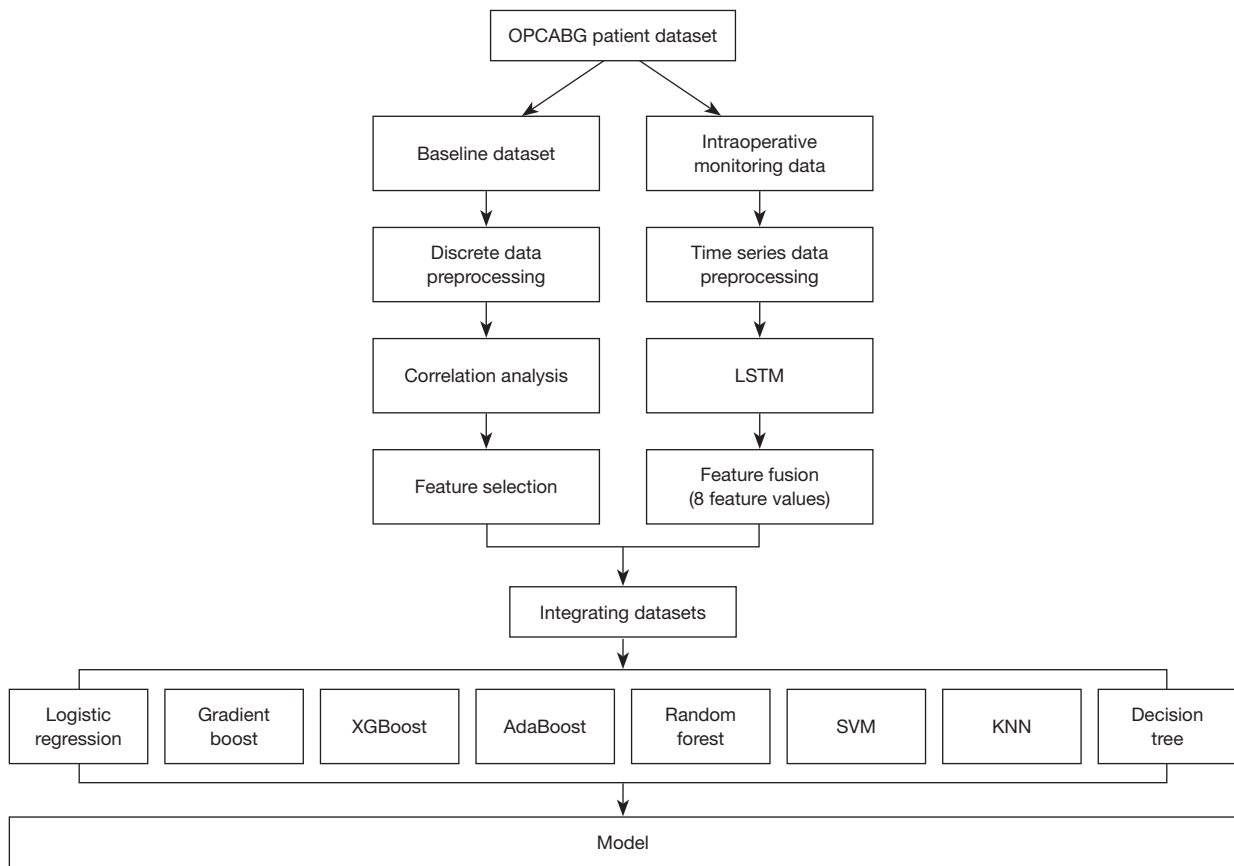
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Figure 1 The statistical analysis plan diagram. OPCABG, off-pump coronary artery bypass grafting; LSTM, long short-term memory; AdaBoost, adaptive boosting; XGBoost, eXtreme gradient boosting; SVM, support vector machine; KNN, k-nearest neighbor.
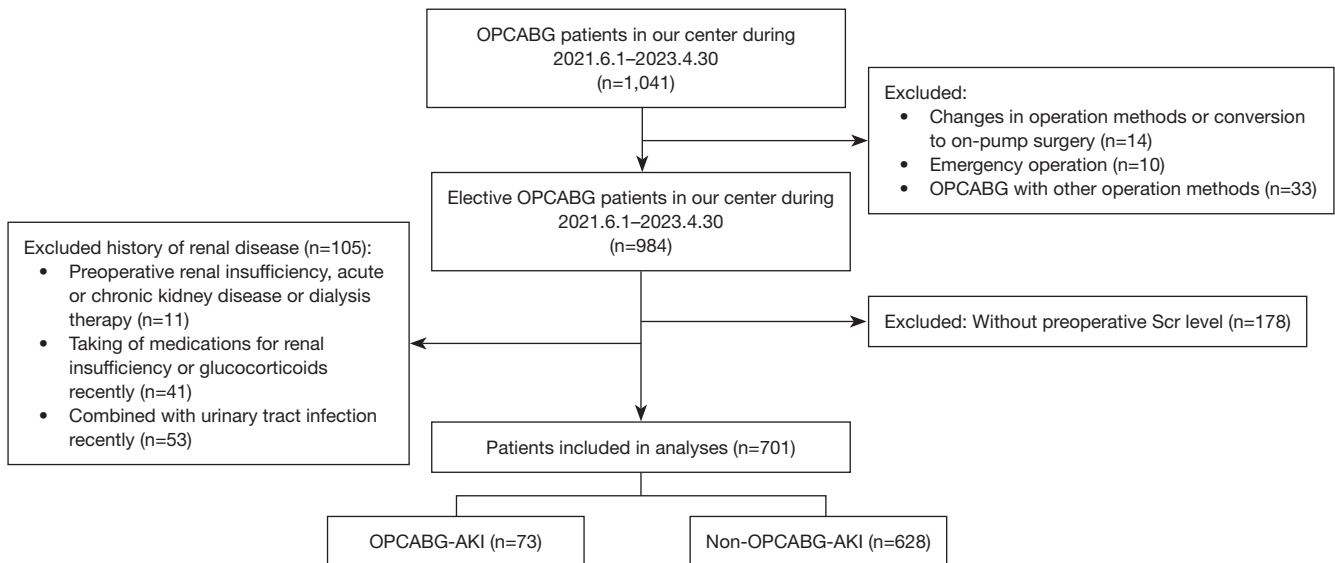

Figure 2 The patients inclusion flowchart. OPCABG, off-pump coronary artery bypass grafting; SCr, serum creatinine; AKI, acute kidney injury.

Table 1 AUC and accuracy of eight machine learning models based on baseline data

Machine learning model	AUC	Accuracy rate
LR	0.717	0.786
SVM	0.731	0.793
DT	0.517	0.871
RF	0.647	0.936
KNN	0.578	0.929
GBDT	0.739	0.943
AdaBoost	0.732	0.907
XGBoost	0.698	0.936

AUC, area under the curve; LR, logistic regression; SVM, support vector machine; DT, decision tree; RF, random forest; KNN, k-nearest neighbor; GBDT, gradient-boosting decision tree; AdaBoost, adaptive boosting; XGBoost, eXtreme gradient boosting.

Figure 3 GBDT model predicts the feature importance ranking of OPCABG-AKI. MI, myocardial infarction; L, left; R, right; CK, creatine kinase; HR, heart rate; SVR, systemic vascular resistance; GBDT, gradient-boosting decision tree; OPCABG-AKI, off-pump coronary artery bypass grafting-associated acute kidney injury.

Table 2 AUC and accuracy rate of eight machine learning models based on baseline and intraoperative datasets

Machine learning model	AUC	Accuracy rate
LR	0.700	0.893
SVM	0.730	0.900
DT	0.550	0.836
RF	0.780	0.921
KNN	0.598	0.936
GBDT	0.861	0.936
AdaBoost	0.726	0.914
XGBoost	0.764	0.936

AUC, area under the curve; LR, logistic regression; SVM, support vector machine; DT, decision tree; RF, random forest; KNN, k-nearest neighbor; GBDT, gradient-boosting decision tree; AdaBoost, adaptive boosting; XGBoost, eXtreme gradient boosting.

Discussion

CSA-AKI is a common complication after cardiac surgery with an incidence rate of up to 1 in 3 patients (18-22), which can lead to increased postoperative mortality, length of hospitalization time, and healthcare costs (23-25). In a meta-analysis including 86 randomized controlled trials (RCTs) and 25,855 patients, 5,082 (20%) patients developed CSA-AKI (11). In addition, the development of kidney disease is accompanied by a high incidence of
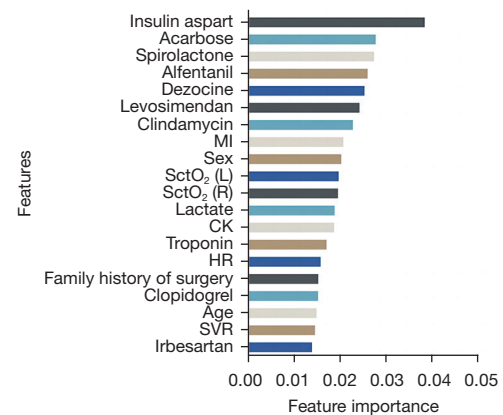
gastrointestinal bleeding and surgical re-exploration for bleeding, respiratory tract infections, and sepsis (26,27). Therefore, the accurate prediction of CSA-AKI before surgery and early detection of high-risk patients can help clinicians to strengthen the physiological and hemodynamic monitoring and provide personalized fluid management at an early stage, which intends to optimize the systemic and renal perfusion in the high-risk patients and reduce the risk of CSA-AKI (28). A number of machine learning models have been developed to predict CSA-AKI. However, there are still no guidelines to recommend predictive models (29). Lee *et al*. (30) showed that XGBoost outperformed traditional LR or risk scores in prediction of CSA-AKI in their study. In another study, an integrated model (RF + XGBoost) was shown with the best performance in prediction of CSA-AKI. However, most models have been limited by heterogeneity of surgery types included, inconsistent definitions of AKI, and different completeness of perioperative data collection. Our present study, which specifically investigated AKI in the setting of OPCABG, determined that a GBDT model had the best predictive performance. Prediction could even be improved further by incorporating intraoperative time series data.

The occurrence of CSA-AKI depends on the patients' preoperative condition and intraoperative physiological processes that are detrimental to the kidneys, including hypotension, low cardiac output syndrome, intraoperative catecholamine surge, decreased vasomotor responsiveness, and others (31). Both preoperative and intraoperative

factors are helpful in prediction of CSA-AKI. Intraoperative features reflect intraoperative physiological changes in the heart. Tseng *et al.* (32) emphasized the value of intraoperative features in prediction of CSA-AKI. A machine learning algorithm was proposed in a single-center cohort study that reclassified approximately 40% of surgical patients; the patients were predicted as low-risk AKI with a preoperative model yet were classified as high-risk after incorporating intraoperative characteristics (33). However, processing intraoperative time series data as the minimum, maximum, average, and short- and long-term variability may result in the loss of the useful information (34). The advantage of our present study was the combination of machine learning and deep learning. Intraoperative features were extracted by a LS-LSTM deep learning model based on intraoperative time series data. Baseline data were subsequently fused with complex features of intraoperative continuous data by means of migration learning, and the integrated data were fed into the machine learning model to predict OPCABG-AKI. Compared with the use of preoperative data alone, the data fusion of baseline data and intraoperative continuous data with complex features improved the accuracy of the GBDT model in the prediction of OPCABG-AKI.

Our findings have some clinical implications. For patients with risk factors of postoperative AKI, although the preoperative factors are difficult to be addressed, the attending surgeons and anesthesiologists would regard these patients as high-risk individuals, focus on their renal function, actively give intervention measures to protect the kidney, closely monitor the hemodynamics, minimize the use of nephrotoxic drugs, and use goal-directed hemodynamic treatment, which would not only ensure effective renal perfusion but also avoid fluid overload. Preoperative variables reflected the baseline characteristics of patients, while intraoperative variables were more closely related to the management of patients by surgeons and anesthesiologists. The intraoperative variables were intraoperative real-time monitoring, and corresponding intervention measures could be taken in time to avoid the occurrence of postoperative AKI. Both of the preoperative baseline characteristics and the intraoperative real-time interventions have significant associations with postoperative AKI.

Previously identified risk factors for CSA-AKI, such as diabetes mellitus, preoperative renal function, age, type of surgery, duration of surgery, left ventricular ejection fraction, body mass index, and hypertension (14,22,35), were not included in the top 20 features for predicting OPCABG-AKI in this study. The main risk factors screened in this study included insulin aspart, acarbose, spironolactone, alfentanil, dezocine, levosimendan, clindamycin, history of myocardial infarction, gender, and others. A total of nine of the top 20 features in the importance of features were medicines used before and during surgery, among which the top five features were all medicines, which suggested that the related drugs can affect the renal function after cardiac surgery.

However, there are certain limitations to our study. Our study only included one single-center nature, and the number of AKI events is relatively small, and there was a lack of external validation and prospective validation. Different stages of AKI were not studied in this study, limited clinical significance. Future studies should include multi-center data, conduct prospective design, and follow up to verify the prediction effect of the model. It may be more beneficial to design observation endpoints for different degrees of AKI to guide clinical practice. Besides, the intra procedural data is lacking, like number of anastomoses, type of grafts. We will include more intra procedural data in our study in the future.

Conclusions

This study demonstrates the applicability of machine learning in predicting the development of OPCABG-AKI. Despite the previous models with AUC >0.7 can be helpful in predicting the risk of AKI following OPCABG, the prediction performance of the present GBDT model is much better. Moreover, the data fusion of preoperative and intraoperative characteristics improved the prediction performance of the GBDT model. The GBDT model may assist clinicians in the risk stratification and clinical decision-making for OPCABG-AKI in these patients who are undergoing OPCABG.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Medical Ethics Committee of Chest Hospital, Tianjin University (No. 2021 KY-008-01). The requirement for informed consent was waived due to the retrospective nature of this study.

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(English Language Editor: J. Jones)

Table S1 Preoperative data

Basic information
• Age
• Height
• Weight
• Level of education
• Work type
• Childbearing
• BMI
• Heart disease history
• Surgical history
• Cardiac surgery history
• Lung disease history
• Kidney disease history
• Liver disease history
• Smoking history
• Drinking history
• Previous myocardial infarction history within 90 days
• Family history of the immediate family
• Diabetes history
• Hypertension history

Physiological index
• Stroke volume—mean
• Tissue oxygen—mean
• Cardiac output—mean
• Right cerebral oxygen—mean
• Heart rate—mean
• Left cerebral oxygen—mean
• Systolic blood pressure—mean
• Left plaque
• Platelet test value
• Systemic vascular resistance—mean
• Diastolic blood pressure—mean
• Mean arterial pressure—mean
• Myoglobin test value
• Hematocrit test value
• Right plaque
• Cr test value
• Albumin test value
• Hemoglobin test value
• Creatine kinase test value
• Uric acid test value
• Troponin T test value
• Hydroxybutyrate dehydrogenase test value

Table S1 *(continued)*

Table S1 *(continued)*

• Aspartate transaminase test value
• Blood urea nitrogen test value
• Anteroposterior diameter of the aortic sinus
• Left atrial diameter
• Alanine transaminase test value
• Interventricular septal thickness
• The left and right basal diameter of the right ventricle
• Lactate dehydrogenase test value
• Left ventricular ejection fraction
• Anteroposterior diameter of the right ventricle
• B-type natriuretic peptide test value
• Pulmonary artery systolic pressure
• Left anterior descending coronary artery
• Left ventricular end diastolic diameter

Evaluation
• Cognitive function
• Chronic lung disease
• Naming skills
• Attention ability
• Linguistic competence
• Abstract ability
• Delayed recall ability
• Orientation ability
• MMSE-score
• Orientation
• Memory
• Attention and numeracy
• Ability to recall
• Language competence
• Nervous system
• EuroScore
• EuroScore-deathrate
• NYHA-rank
• Metabolic disease
• Nervous system dysfunction
• Left ventricular dysfunction with LVEF 30–50%
• Diseases of the extracardiac arterial system
• Visuospatial/executive ability
• Unstable angina requiring medical intervention
• Metabolic equivalent of task score

BMI, body mass index; Cr, creatinine; MMSE, minimum mental state examination; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction.