Preoperative 6-Minute Walk Distance Is Associated With Postoperative Cognitive Dysfunction

Kazuhiro Hayashi, PT, MS, Hideki Oshima, MD, PhD, Miho Shimizu, PT, MS, Kiyonori Kobayashi, PT, MS, Shigeyuki Matsui, PhD, Yoshihiro Nishida, MD, PhD, and Akihiko Usui, MD, PhD

Department of Rehabilitation, Nagoya University Hospital, Nagoya; Multidisciplinary Pain Center and Department of Rehabilitation, Aichi Medical University, Nagakute; and Departments of Cardiac Surgery, Biostatics, and Orthopedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan

Background. **Postoperative cognitive dysfunction (POCD) is a neurologic dysfunction that occurs after surgery. POCD persists for a long period, ranging from weeks to months, and affects a patient's quality of life. A 6-minute walk distance (6MWD) has been used to predict postoperative complications after several operations. The present study investigated whether there was an independent association of a low preoperative 6MWD with POCD in patients who underwent cardiac operations.**

Methods. **The study included 181 patients who underwent a cardiac operation. The 6MWD was performed prospectively on admission for the operation. POCD was defined as a decrease of 2 points or more in a patient's Mini-Mental State Examination score. POCD developed in 51 (28%) of these patients. Patients were categorized into a POCD or a non-POCD group, and the perioperative variables were compared between the groups. Multivariable logistic regression analysis was performed to identify risk factors for the development of POCD.**

Results. **The patients were a mean age of 71.4 years. The POCD group showed a significantly lower 6MWD (median, 400 m) than the non-POCD group (median, 450 m). The 6MWD, intensive care unit length of stay, age, and Mini-Mental State Examination score were identified as independent risk factors for POCD by multivariable analysis. The odds ratio for each increase of 50 m in the 6MWD was 0.807 for POCD.**

Conclusions. **The 6MWD is useful in identifying patients with a higher chance of developing POCD after a cardiac operation.**

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Postoperative neurologic dysfunction is a concern because it affects patients' quality of life and has implications for health economics [1]. Postoperative cognitive dysfunction (POCD) is one of the neurologic dysfunctions that persists the longest, often for weeks to months after surgery [2]. POCD is usually reversible; however, in certain cases, POCD can be long-lasting [2]. The incidence of POCD ranges from 50% to 70% within 1 week after a cardiac operation and falls to 30% to 50% after 6 weeks and to 20% to 40% at 6 months and 1 year [1].

The definition of POCD remains controversial, and many definitions have been used [1, 3]. The Mini-Mental State Examination (MMSE) is often used to measure cognitive change over time in older adults [4]. Reliable changes in MMSE scores for short intervals correspond to a loss of at least 2 points [4–8]. Several studies defined POCD as a reduction in MMSE of at least 2 points from baseline several days after the operation [5–8]. The assessment timing of POCD begins as soon as 1 day after the operation and can extend to as long as 5 years later [3]. The incidence of POCD is highest at discharge, often between 5 and 15 days postoperatively [1]. In addition, other postoperative functional disabilities are often assessed approximately 2 weeks after cardiac operations [9, 10].

A precise preoperative risk assessment for postoperative complications is critical for determining the operative indication and planning a perioperative patient management strategy. Risk factors for POCD after cardiac operations include older age [3] and preoperative cognitive impairment [3]. The 6-minute walk test is a simple, safe, and inexpensive test that can be used for evaluating patients' functional exercise capacity [11]. Recently, the preoperative 6-minute walk distance (6MWD) has also been used to predict complications after several different surgical procedures [12–15].

The reduction of cardiorespiratory reserve is believed to lead to the development of tissue hypoxia, the basis for multiple organ failure and postoperative complications [16]. In patients scheduled for cardiac operations, a low preoperative 6MWD identifies patients who will require a longer rehabilitation stay [10]. Recent systematic reviews concluded that poor physical function, such as frailty, was

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Address correspondence to Kazuhiro Hayashi, Nagoya University Hospital, 65 Tsuruma-cho, Showa-ku, Nagoya, Japan; email: hayashi.kzhr@gmail.com.

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associated with death and with cardiac and cerebral vascular events after cardiac operations [17]. To the best of our knowledge, however, the relationship between preoperative physical function and POCD has not been investigated to date. The results of the preoperative 6MWD may indicate a higher chance of developing postoperative neurologic dysfunction after cardiac operations.

The purpose of the present study was to investigate whether there was an independent association of low preoperative 6MWD with POCD in patients who underwent cardiac operations.

Patients and Methods

Participants

A total of 305 consecutive patients undergoing an elective cardiac operation (coronary artery bypass graft, valve replacement, a thoracic aortic operation, or a combination of these) who could be assessed in a preoperative walking test between March 2014 and August 2015 at Nagoya University Hospital, Japan, were eligible to participate in this study. Patients who were younger than 60 years (n = 70) were not included in the study because they had a low incidence of POCD [18]. Patients were not included in the study if they had a score on the MMSE of less than 24 (n = 31), similar to previous studies [5–7]. Patients with significant cognitive impairment have made the exercise assessment unreliable [19] and limited the indication for the operation.

There were no patients with central nervous system diseases, such as Parkinson disease, or severe hearing or vision disorders. Of the remaining 204 patients, patients were not included in the analysis if they had suffered from postoperative cerebral stroke (n = 4), could not be assessed due to postoperative hemodynamic instability (n = 7), gastrointestinal complications (n = 5), pneumonia (n = 2), mediastinitis (n = 1), cardiac tamponade (n = 1), or paraplegia (n = 1), or were discharged before completing the cognitive function test (n = 2). These 23 patients could not be assessed for postoperative MMSE because they had decreased consciousness, unstable hemodynamics, severe pain, or rejected the measurement. As shown in Figure 1, we finally included 181 patients who underwent coronary artery bypass graft (n = 64), valve replacement (n = 81), or an aortic operation (n = 36).

Our hospital administered standardized inpatient treatment after the operation [20]. MMSE and 6MWD measurements were routinely taken for all patients during the inpatient period. All patients were provided with similar preoperative and postoperative rehabilitation, which included mobilization, ambulation, breathing, and muscle strengthening exercises.

During the surgical procedure, mean arterial pressure was maintained between 50 and 80 mm Hg and was maintained above 70 mm Hg in patients with cerebral vascular stenosis. The transfusion threshold was set at a hemoglobin level of 7 to 8 g/dL. Cerebral oxygen saturation was monitored to maintain above the baseline value using an INVOS oximeter (Covidien, Mansfield, MA). The intensive care unit (ICU) doctors and nurses are present in this closed ICU unit all day. Extubation was performed whenever possible. Preanesthetic medication is not administered at our hospital.

The Nagoya University Hospital Ethics Committee approved this study (N0.0197). All patients provided informed consent to participate in this study.

Evaluation of the 6MWD

Functional exercise capacity was measured using the 6MWD on admission for the operation. The 6MWD evaluation was performed prospectively in consecutive patients who underwent elective cardiac operations. The 6-minute walk test was performed by following a standardized procedure [21]. Briefly, patients were instructed to walk the length of a predetermined course at their own pace while attempting to cover as much ground as possible in 6 minutes. Standardized encouragement was given each minute during the test. At the end of the 6 minutes, patients were instructed to stop walking, and the distance covered was measured to the nearest meter.

Data Collection

Demographic data, including age, sex, height, body weight, body mass index, and other comorbidities, were recorded. The Charlson comorbidity index was used to uniformly score comorbid conditions [22]. The presence of preoperative anemia was defined as hemoglobin of less than 12 g/dL for women and less than 13 g/dL for men preoperatively [23]. Also recorded were intraoperative data such as surgical procedure, operative time, anesthesia time, intraoperative blood loss, perioperative transfusion, cardiopulmonary bypass time, aortic cross-clamp time, and the presence of circulatory arrest. Perioperative transfusion was defined as at least 1 unit of packed or whole red blood cells given at any point from the start of the operation up to 72 hours postoperatively.

Postoperative complications, ICU and hospital length of stay, and transfer to another hospital were recorded. Decisions regarding ICU and hospital discharge were made by attending physicians in collaboration with other members of the care team [24]. Sedation was assessed using the Richmond Agitation-Sedation Score [25]. The MMSE was measured on admission and at 2 weeks postoperatively (mean, 12.9 ± 1.9 days postoperatively). The MMSE was assessed in more than half of the patients (n = 129) at 14 ± 2 days postoperatively; meanwhile, 48 patients were assessed before day 12 because of the prospect of early discharge, and 4 patients were assessed after 16 days because of scheduling issues. All patients were assessed before hospital discharge. POCD was defined as a significant decline in cognitive function based on a decrease of 2 or more in the MMSE score [5–8].

The sample size was calculated based on a two-sided, two-sample *t* test using G*Power 3.0.10 software (Franz Faul, Kiel University, Kiel, Germany). On the basis of the within-group SD, 100 m, the expected mean difference in