Early and Late Outcomes of Thoracic Aortic Surgery in Hemodialysis Patients

AORTIC SURGERY IN HEMODIALYSIS PATIENTS

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Background: The number of cardiovascular surgeries in hemodialysis patients is increasing according to the growing population of hemodialysis patients, however, the clinical outcome has not yet been clarified, especially in thoracic aortic surgery. The purpose of this study was to assess the early and late outcomes of thoracic aortic surgery in hemodialysis patients.

Methods: We retrospectively analyzed the outcomes of 700 consecutive open thoracic aortic surgeries from 2002 to 2014. We identified 21 patients on preoperative hemodialysis (Group HD) and 679 patients without preoperative hemodialysis (Group N). The patients were predominantly male, had diabetes and cardiogenic shock, and had less hyperlipidemia and elective surgery in Group HD. The early and late outcomes were compared between 21 patients in each group using a propensity-score matched analysis.

Results: The hospital stay and intensive care unit stay were significantly longer in Group HD even after matching. The 30-day mortality and in-hospital mortality showed no significant differences, whereas the rate of postoperative pneumonia was significantly higher in Group HD compared with the matched Group N (p=0.0067). The 1-, 3- and 7-year survival rates in Group HD were 73.4%, 45.7% and 30.5%, respectively, which were significantly poorer than that of Group N both in the pre-matched (p<0.001) and matched analyses (p=0.025).

Conclusions: Considering the various operative risks associated with hemodialysis patients, the early mortality rate is acceptable, even after the association with many respiratory complications. Although hemodialysis patients have a compromised prognosis after surgery, excessive hesitation to perform thoracic aortic surgery may be avoided.

249 words

Introduction

The number of patients receiving hemodialysis (HD) has increased annually, which is becoming a worldwide trend. In Japan and the United States, rather than the recent plateau in the incident rate of dialysis (285 and 349 per million per year in 2012, respectively), the prevalence of dialysis continues to increase (2431 and 1403 per million per year in 2012, respectively; HD accounted for 96.9% and 91.0% of these cases, respectively) [1, 2]. Because cardiovascular death is the most common cause of death in dialysis patients in Japan and the United States (33.5% and 41.6% of all deaths in 2012, respectively), followed by infection death (25.7% of all deaths in 2012 in Japan) [1, 2], we cardiovascular surgeons thus play an important role in the improvement of their survival. The need to understand the results of cardiovascular surgery for HD patients is becoming higher due to the growing population of HD patients. There have been reports about the outcome of abdominal aortic aneurysm (AAA) repair in dialysis patients [3]. However, few data exist regarding thoracic aortic (TA) surgery in HD patients thus far, because the number of the cases is limited [4]. In this study, we assessed the early and late outcomes of TA surgery in HD patients compared with patients without HD.

Methods

We retrospectively analyzed the records of 700 consecutive open TA surgeries from January 2002 to October 2014 at our institution. The study was approved by the Institutional Review Board of Nagoya University Graduate School of Medicine. We identified 21 patients (3%) who had preoperatively undergone HD (Group HD) and compared them with 679 patients (97%) without preoperative HD (Group N). No patient received peritoneal dialysis, and no patients were excluded from this cohort.

Various operative techniques were used for TA surgery according to aortic disease and anatomy. Among the 21 patients in Group HD, open surgery for the aortic root was performed in 2, ascending aorta in 6 and aortic arch in 6 patients solely via median sternotomy (n=14), while left thoracotomy was performed for the extended aortic arch in 1, descending aorta in 5 and thoracoabdominal aorta in 1 patient (n=7). The pathology of aortic lesions included 8 true aneurysms, 4 pseudoaneurysms, 4 acute dissections, 3 chronic dissections, and 2 severely calcified aortas. Nine patients underwent surgery in an emergency or urgent situation, and only 12 patients had elective surgery. Six patients had a history of previous cardiovascular surgery including coronary artery bypass grafting (CABG) in 1, total arch replacement in 2, thoracoabdominal aortic replacement in 1, open abdominal aortic replacement in1 and both total arch replacement and thoracoabdominal aortic replacement in 1 patient. In Group HD, the mean duration of HD was 3.4±7.0 years, and the causes of dialysis were nephrosclerosis in 9, diabetic nephropathy in 6, renovascular disease in 2, glomerular nephritis in 2 and lupus nephritis in 1 patient. In Group N, the average preoperative serum creatinine level was 0.95±0.42 (range 0.26-5.06) mg/dl.

There were six significant differences in the preoperative factors in the pre-matched groups (Table 1). In Group HD, the rates of male sex, diabetes, liver dysfunction and cardiogenic shock were significantly higher and hyperlipidemia and elective surgery were significantly lower than that of Group N. The proportion of patients who had a history of previous cardiovascular surgery was not significantly different between both groups (6, 28.6% vs 200, 29.5%, respectively; p=0.91). In Group HD, there were many concomitant procedures, however, no significant differences were observed. The rate of emergency operation was significantly higher in Group HD, however, HD patients did not have significantly more emergency or urgent operations for acute dissection (4, 19.1% in Group HD vs 91, 13.4% in Group N; p=0.46) or pseudoaneurysm (1, 4.8% in Group HD vs 5, 0.74% in Group N; p=0.17). To compare the two groups, we used a propensity-score matching analysis adjusting for the difference in the patient characteristics and the number of patients. To assess the influence of emergency surgery, we compared the patients in Group HD who underwent elective surgery with those who underwent non-elective surgeries.

Statistical Analysis

Statistical analyses were performed using the JMP pro version 11 software program (SAS Institute, Cary, NC). Continuous variables are expressed as the means ±1 standard deviation or the median (interquartile range) and were compared using t-tests. Categorical variables are expressed as the counts and percentages and were compared using Pearson's X2 analysis or Fisher's exact test.

Propensity-score matching was used to account for nonequivalence in the baseline characteristics between Group HD and Group N for seven characteristics (sex, diabetes, hyperlipidemia, liver dysfunction, elective vs non-elective surgery, smoking history, and obesity), as mentioned above. The matching variables for propensity-score matching were chosen according to significant preoperative differences between Group HD and Group N or variables adjusting for differences in the preoperative characteristics. We first utilized sex, diabetes, hyperlipidemia, liver dysfunction, and elective surgery as matching variables; cardiogenic shock was excluded as a matching variable because of its strong relationship with elective surgery. After matching, significant differences in the patient characteristics remained, which were obesity and smoking history. We subsequently added these two variables as matching variables to eliminate the differences in the patient characteristics. Propensity scores were estimated using logistic regression modeling with the likelihood for HD. To include all HD patients in the propensity-score matching analysis, we used a caliper of 0.8 for the short-term result analysis of all patients. The postoperative outcomes were then compared between matched groups using the paired t-test and Wilcoxon's signed rank test for continuous variables and McNemar's test for categorical variables.

Kaplan-Meier curves were created to estimate the long-term survival for the pre-matched and matched groups. Differences between the groups were compared using the log-rank test for the pre-matched two-group analysis and the stratified log-rank test for the matched two-group analysis. All statistical tests were two-sided with $p<0.05$ considered to be statistically significant.

Results

Short-term results in 21 patients with preoperative hemodialysis (Group HD)

In Group HD, 7 patients required reintubations, which were due to pneumonia in 6 and glottis edema in 1, and 5 resulted in tracheotomy. The other HD patient required tracheotomy after the management of pneumonia via percutaneous cricothyroidostomy (minitracheostomy) without reintubation. Gastrointestinal (GI) complications included bleeding from a gastric ulcer, perforation of the esophagus potentially due to the operative maneuver, mesenteric ischemia and obstructive colitis due to elongation of the sigmoid colon. There were three hospital deaths in Group HD; 2 were due to sepsis by mesenteric ischemia or obstructive colitis and 1 was due to pneumonia.

Comparison of the short-term results in the pre-matched groups

The average postoperative hospital stay and intensive care unit (ICU) stay were significantly longer in Group HD (Table 2). Although there was no significant difference in the number of postoperative initial ventilation hours between the two groups, the frequency of postoperative pneumonia and tracheotomy was significantly higher in Group HD (both $p<0.0001$). The occurrence of GI complications and groin surgical wound infection was also significantly higher in Group HD ($p=0.0087$ and $p=0.0081$, respectively). Although not significant, the in-hospital mortality was relatively higher in Group HD (14.3%).

Comparison of the short-term results in the propensity-score matched groups

As described in the Methods, we conducted propensity-score matching to eliminate preoperative differences in the two groups to compare the surgical outcomes. Twenty-one patients from each group were matched for seven preoperative factors (Table 1). The pair-matched statistical analysis did not demonstrate any differences in the number of initial ventilation hours, however, the average postoperative hospital stay and ICU stay were significantly longer in Group HD (p=0.030 and p=0.033, respectively) (Table 2). Additionally, postoperative pneumonia occurred more frequently in Group HD. The reintubation rate was also significantly higher in Group HD (7, 33.3% in Group HD vs 1, 4.8% in Group N; p=0.034). However, no significant differences were observed in the mortality or other postoperative complications.

Long-term results in the pre-matched groups

The completion rate of follow-up was 89.0%. During an average follow-up of 43.0±38.1 months, there were 7 late deaths in Group HD. These were caused by cardiovascular deaths in 5 cases, including congestive heart failure in 2, thoracic aortic aneurysm rupture due to an infectious aortic aneurysm in 1, AAA rupture in 1 and sudden death in 1 patient. The other 2 deaths were due to sepsis in 1 and unknown death in 1 patient. We calculated the Kaplan-Meier estimates of the survival to assess the long-term survival (Figure 1). The 1-, 3- and 7-year survival rates were 73.4%, 45.7%, 30.5% in Group HD and 92.0%, 86.3%, 74.0% in Group N, respectively, which was significantly different (log-rank $p<0.001$ for all).

Long-term results in the propensity-score matched groups

The Kaplan-Meier estimates of the survival were calculated to assess the long-term results of the propensity-score matched Group N (Figure 1). The 1-, 3- and 7-year survival rates were 100%, 91.7% and 91.7%, respectively. To compare the long-term results, the stratified log-rank test was performed, which showed that the survival was significantly different between the two matched groups ($p=0.0027$).

Effect of non-elective surgeries in Group HD

A comparison between patients who underwent elective and non-elective surgeries in Group HD showed no significant difference in the early results except for perfusion time ($p=0.039$) (Table 3). The estimated survival curve did not show any significant difference (Figure 2).

Comments

Aortic diseases and hemodialysis patients

Renal failure requiring HD is known to cause systemic arteriosclerosis, cardiovascular diseases and a decreased survival rate [5-8]. In addition to impaired calcium and phosphate metabolism causing coronary artery calcification and valve and annulus calcification [9-11], arterial remodeling causing arterial enlargement is thought to occur in the course of renal failure by chronic blood volume/flow overload (anemia, arteriovenous shunts and sodium and water retention) or endothelium impairment by the uremic status rather than lipid abnormalities, both resulting in arterial stiffening [7]. The high incidence of aortic dilation in children with end-stage renal disease is suggestive of a similar etiology [12]. Previous studies have also shown the relationship between aortic aneurysms and arterial calcification, which increased by HD duration [5, 9].

Reports about aortic surgery in HD patients are scarce, particularly regarding TA surgery. This may be because the frequency of aortic surgery in HD patients is low. This, in turn, might be related to delayed decision-making for operation, which is affected by the potentially high mortality or frailty of HD patients, or the small population of HD patients with aortic aneurysms, which is strongly affected by the poor prognosis of the HD population rather than the tendency to dilate the aorta. The proportion of dialysis patients was only 1.8% of patients who underwent elective surgery for a nondissectional ascending aorta and aortic arch using cerebral protection according to a study using the Japanese adult cardiovascular surgery database [4]. In the present study, the proportion of HD patients among all patients who received TA surgery was 21 out of 700 (3.0%), which was significantly lower than those who received major cardiovascular surgery, excluding TA surgery, during the same period in our institution (107 out of 1968 patients, 5.4%; p=0.0096). Yuo et al. described that considering the higher 30-day mortality of AAA surgery in dialysis patients and the poor life expectancy of patients with both AAA and dialysis, the use of the aneurysm size to determine the indications for surgery may need to be raised [3].

To determine whether TA surgery in HD patients is valid for operations such as CABG [13-16] and valve surgery [17-19], we herein described the result of TA surgery in HD patients in the real-world setting. We used the propensity-score matching analysis to compare the postoperative results of patients with and without HD in this retrospective study in order to eliminate preoperative bias.

Preoperative characteristics

Age, male sex, diabetes, hypertension, obesity, hyperlipidemia, and smoking are the risk factors for renal failure in the general population [20], however, most of these factors are also risk factors for aortic aneurysms. While the frequency of male sex and diabetes was significantly higher in Group HD in this population, hyperlipidemia and obesity were higher in Group N, which might represent the chronic malnutrition status of HD patients.

Operative management and early and long-term results

In the initiation of cardiopulmonary bypass, careful attention for potential arterial calcification or thrombus is needed to avoid cannulation site issues, organic malperfusion or emboli. Handling of the fragile anatomy including a severely calcified aorta and adequate control of the fluid balance, electrolytes and acidosis before the termination of cardiopulmonary bypass are crucial in aortic surgeries for HD patients. These factors were speculated to require a longer perfusion time in HD patients, however, there was no significant difference.

Even after matching, the ICU stay was significantly longer in Group HD. This may be the result of the frail, compromised immune function and malnutrition of HD patients during the intubation period, resulting in high rates of pneumonia and tracheostomy. In addition, careful postoperative fluid removal, and the limited availability of HD outside of the ICU, due to the capacity of the HD facility in our hospital, might have prolonged the ICU stay, even for patients without pneumonia.

The mortality rate was higher in Group HD, but this difference was not significant. The small number of patients in Group HD in this study might have failed to confirm the high mortality of HD patients receiving aortic surgery, which was shown in a previous study [21]. Additionally, a high rate of emergency and concomitant surgeries in Group HD may result in a poor short-term mortality [21, 22], although this study did not show significantly different results between patients who underwent elective and non-elective surgeries in Group HD, possibly due to the small numbers.

The long-term survival of Group HD was significantly poorer than that of Group N both in the pre-matched and propensity-score matched analyses. HD patients had many preoperative factors that could cause worse outcomes, such as male sex, diabetes and a critical preoperative status. After adjusting for the preoperative factors, the survival rate was still worse in HD patients. This finding may have resulted from the poor expected survival curve of HD patients. However, we must consider that almost half of the patients underwent non-elective surgery and would not have survived without an aortic operation. Moreover, the survival curve of Group HD without hospital death (the 1-, 3- and 7-year survival rates were 87.1%, 54.2% and 36.2%, respectively) was nearly comparable to those of the general population of dialysis patients, although we could not compare these groups due to the different backgrounds (the 1-, 3- and 7-year survival rates were 85.1%, 70.0% and 47.2%, respectively, in Japan and the 1-, 3-, 5-year survival rates were 76.4%, 54.9% and 40.4%, respectively, in the United States) [1, 2]. Considering the aforementioned fact, the indications for operation may not need to be largely amended from our current standard practice.

TA surgery for HD patients is associated with frequent emergency operations and a higher rate of respiratory complications, thus the surgical strategy and postoperative management for HD patients must be sophisticated to minimize the risk of operations.

Limitations

There are some limitations associated with the present study. First, the present study was retrospective and performed at a single institutional. Additionally, the number of HD patients was small. Thus, in addition to the weakened power of the study, a potential selection bias may exist, although the two groups were compared using propensity-score matching. All patients who consulted our department underwent surgical treatment, however, we cannot deny the possibility that some patients were not offered surgical options in a local clinic or department of internal medicine before our surgical department was consulted.

Conclusions

Considering the various operative risks in many emergency operations in HD patients, the early mortality rate was acceptable even after the association with many respiratory complications. Although HD patients have a compromised prognosis after surgery, excessive hesitation to perform TA surgery may be avoided.

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Table 1. Preoperative and Operative Characteristics Before and After Propensity-score Matching

Variable	Group HD (n=21)		Pre-matched Group N (n=679)		p value	Propensity-score matched Group N (n=21)		p value
Age at operation (years)	63.3	±15.5	65.7	±13.0	0.42	60.3	±16.0	0.60
Male sex (%)	20	(95.2)	468	(68.9)	0.007	20	(95.2)	1
Smoking history (%)	10	(47.6)	374	(55.1)	0.50	10	(47.6)	1
Diabetes (%)	9	(42.9)	79	(11.6)	<0.0001	9	(42.9)	1
Hypertension (%)	14	(66.7)	496	(73.1)	0.52	18	(85.7)	0.21
Hyperlipidemia (%)	2	(9.5)	216	(31.8)	0.031	1	(4.8)	0.32
Obesity (%)	1	(4.8)	136	(20.0)	0.096	2	(9.5)	0.32
Cerebral vascular disease (%)	3	(14.3)	79	(11.6)	0.73	4	(19.1)	0.65
COPD (%)	1	(4.8)	64	(9.4)	0.71	1	(4.8)	1
Liver dysfunction (%)	2	(9.5)	8	(1.2)	0.033	2	(9.5)	1
Immunosuppressant (%)	2	(9.5)	33	(4.9)	0.28	0	(0)	
Low EF <30 (%)	1	(4.8)	8	(1.2)	0.24	0	(0)	
Dissection (%)	7	(33.3)	241	(35.5)	0.84	10	(47.6)	0.26
Elective surgery (%)	12	(57.1)	544	(80.1)	0.010	14	(66.7)	0.16
NYHA >3 (%)	2	(9.5)	27	(4.0)	0.21	0	(0)	0.48
Cardiogenic shock (%)	3	(14.3)	15	(2.2)	0.014	0	(0)	0.25
Concomitant surgery (%)	9	(42.9)	180	(26.5)	0.10	3	(14.3)	0.083
Valve (%)	7	(33.3)	119	(17.5)	0.12	0	(0)	
CABG (%)	4	(19.0)	56	(8.3)	0.18	3	(14.3)	0.71
Other (%)	1	(4.8)	26	(3.8)	0.57	0	(0)	
Median sternotomy (%)	14	(66.7)	485	(71.4)	0.63	15	(71.4)	0.74
Range of replacement					0.30			0.33
Root - Asce (%)	8	(38.1)	173	(25.5)		4	(19.1)	
Arch (%)	7	(33.3)	334	(49.2)		11	(52.4)	
Des - ThoAbd (%)	6	(28.6)	172	(25.3)		6	(28.6)	

Variables are expressed as the mean ± standard deviation or number (%).

Asce = ascending aorta, CABG = coronary artery bypass grafting, COPD = chronic obstructive pulmonary disease, Des = descending aorta, EF = ejection fraction of the left ventricle, NYHA = New York Heart Association, ThoAbd = thoracoabdominal aorta.

Table 2. Early Results Before and After Propensity-score Matching

Variable	Group HD (n=21)	Pre-matched Group N (n=679)	p value	Propensity-score matched Group N (n=21)	p value
Perfusion time (minutes)	210 (169.5-281)	207 (163-265)	0.43	196 (164.4-311.5)	0.87
ICU stay (days)	7 (3-14)	3 (2-7)	0.033	5 (2-7)	0.049
Hospital stay (days)	41 (24.5-105.5)	29 (21-42)	0.030	29 (20-33.5)	0.012
In-hospital mortality (%)	3 (14.3)	26 (3.8)	0.051	0 (0)	
30-day mortality (%)	1 (4.8)	14 (2.0)	0.38	0 (0)	
Ventilation (hours)	65 (18.5-204)	31 (11-106)	0.99	68 (16.5-156)	0.62
Ventilation >24 hours (%)	14 (66.7)	352 (51.8)	0.18	12 (57.1)	0.48
Ventilation >72 hours (%)	9 (42.9)	232 (34.2)	0.41	9 (42.9)	1
Pneumonia (%)	11 (52.4)	77 (11.3)	<0.0001	2 (9.5)	0.0067
Tracheotomy (%)	6 (28.6)	33 (4.9)	<0.0001	0 (0)	
Transfusion (%)	21 (100)	607 (89.4)	0.15	18 (85.7)	
Reoperation for bleeding (%)	1 (4.8)	51 (7.5)	1	1 (4.8)	1
Reoperation for sternum (%)	1 (4.8)	10 (1.5)	0.29	1 (4.8)	1
Cardiac tamponade (%)	0 (0)	31 (4.6)	0.62	2 (9.5)	
GI complication (%)	4 (19.1)	25 (3.7)	0.0087	1 (4.8)	0.18
Stroke (%)	3 (14.3)	74 (10.9)	0.50	3 (14.3)	1
Mediastinitis (%)	0 (0)	6 (0.9)	1	0 (0)	
Thoracotomy infection (%)	1 (4.8)	14 (2.1)	0.37	0 (0)	
Groin infection (%)	2 (9.5)	3 (0.4)	0.0081	0 (0)	
Septicemia (%)	2 (9.5)	27 (4.0)	0.21	0 (0)	
Atrial fibrillation (%)	4 (19.1)	184 (27.1)	0.62	5 (23.8)	0.71

Variables are expressed as the median (interquartile range) or number (%).

GI = gastrointestinal, ICU = intensive care unit.

Table 3. Early Results of Group HD between Elective and Non-elective Patients

Variable	Group HD elective (n=12)	Group HD non-elective (n=9)	p value
Perfusion time (minutes)	199 (140.75-241.5)	269 (177-403.5)	0.039
ICU stay (days)	7.5 (3-18.75)	7 (4-11.5)	0.34
Hospital stay (days)	42.5 (25.25-100.25)	35 (16.5-112.5)	0.94
In-hospital mortality (%)	1 (8.3)	2 (22.2)	0.55
30-day mortality (%)	0 (0)	1 (11.1)	0.43
Ventilation (hours)	37.5 (17.75-195.75)	90 (40.5-204)	0.51
Ventilation >24 hours (%)	7 (58.3)	7 (77.8)	0.64
Ventilation >72 hours (%)	4 (33.3)	5 (55.6)	0.40
Pneumonia (%)	8 (66.7)	3 (33.3)	0.20
Tracheotomy (%)	5 (41.7)	1 (11.1)	0.18
Reintubation (%)	6 (50)	1 (11.1)	0.16

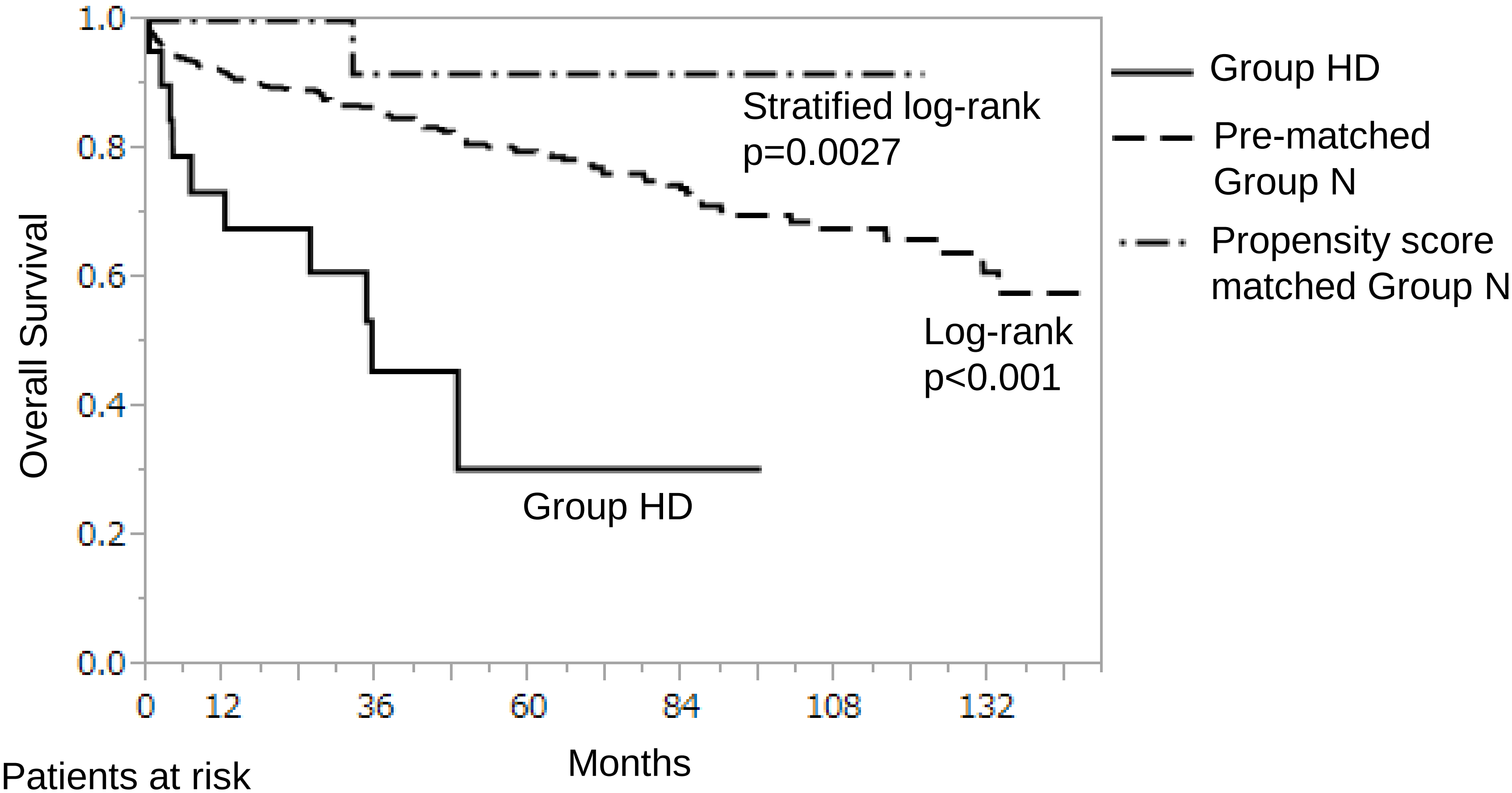
Variables are expressed as the median (interquartile range) or number (%).

ICU = intensive care unit.

Figure 1. The estimated overall survival rate of Group HD and Group N between before and after matching.

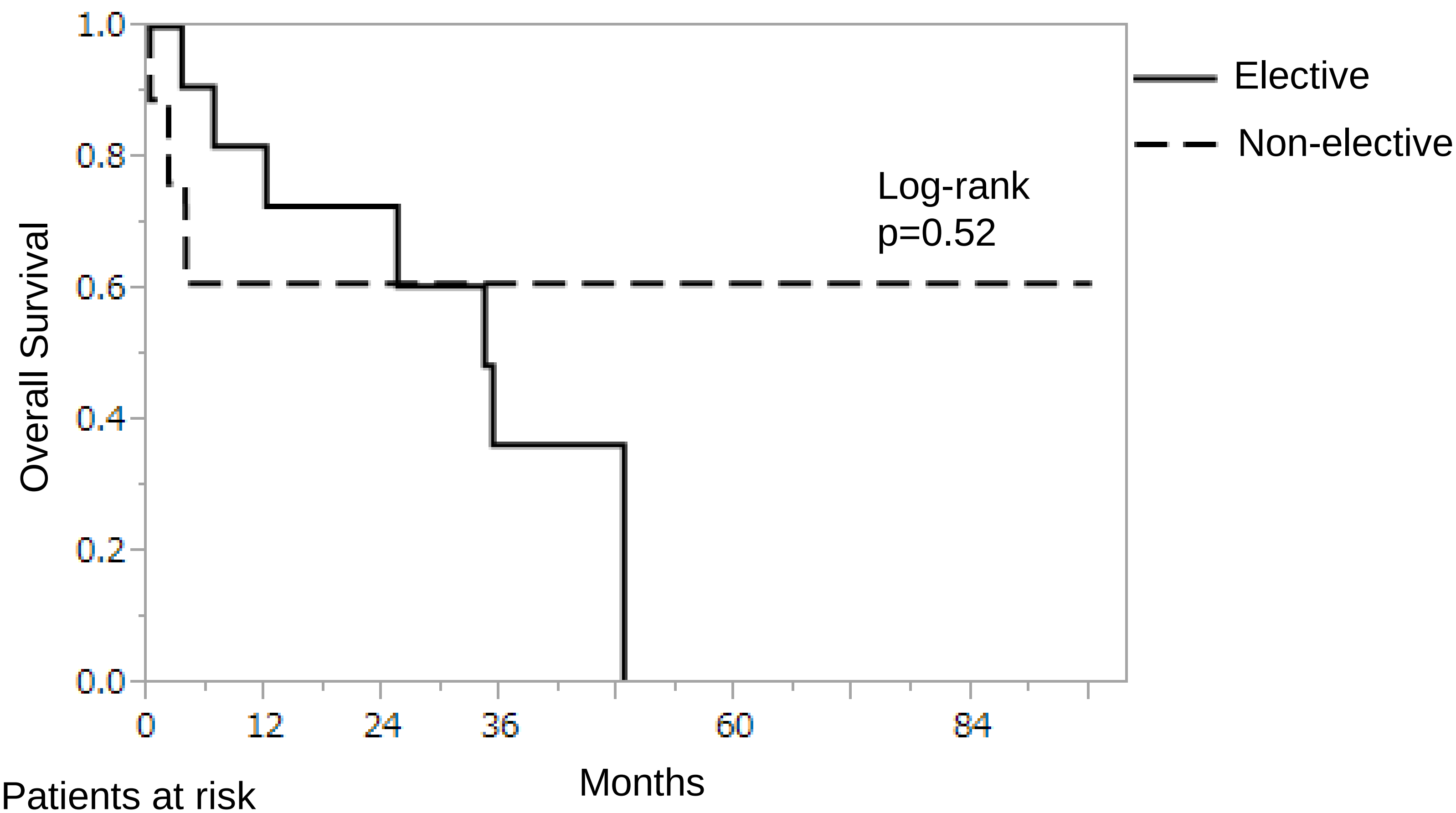
Figure 2. The estimated overall survival rate of Group HD between elective and non-elective patients.

Figure 1



Patients at risk						
Group HD	**21**	**14**	**7**	**3**	**2**	
Pre-matched Group N	**679**	**498**	**321**	**201**	**119**	**55**
Matched Group N	**21**	**16**	**10**	**4**	**4**	**2**

Figure 2



Patients at risk

Elective	**12**	**10**	**7**	**4**
Non-elective	**9**	**5**	**5**	**4**