Prestroke glycemic control is associated with the functional outcome in acute ischemic stroke : The Fukuoka Stroke Registry

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Prestroke glycemic control is associated with the functional outcome in acute ischemic stroke. The Fukuoka Stroke Registry.

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Abstract

***Background and Purpose*:** Diabetes mellitus is an established risk factor for stroke. However, it is uncertain whether the prestroke glycemic control (PSGC) status affects the clinical outcomes of acute ischemic stroke. The aim of this study was to elucidate the association between the PSGC status and neurological or functional outcomes in patients with acute ischemic stroke.

***Methods*:** From the Fukuoka Stroke Registry, a multicenter stroke registry in Japan, 3627 patients with a first-ever ischemic stroke within 24 hours after onset were included in the present analysis. The patients were categorized into four groups based on their PSGC status: excellent (hemoglobin A1c on admission <6.2%), good (6.2-6.8%), fair (6.9-8.3%) and poor (≥8.4%). Study outcomes were neurological improvement (≥4 points of decrease in the National Institutes of Health Stroke Scale (NIHSS) score during hospitalization or zero point on the NIHSS score at discharge), neurological deterioration (≥1 point increase in the NIHSS score) and poor functional outcome (death or dependency at discharge, modified Rankin Scale of 2 to 6).

***Results*:** The age- and sex-adjusted odds ratios for neurological improvement were lower, and those for neurological deterioration and a poor functional outcome were higher in the patients with a poorer PSGC status. After adjusting for multiple confounding factors, these trends were unchanged (all p values for trends were <0.002). These findings were comparable in patients with non-cardioembolic and cardioembolic infarctions.

Conclusions: In ischemic stroke patients, the HbA1c on admission was an independent significant predictor for the neurological and functional outcomes.

Introduction

Diabetes is an established risk factor for the development of cardiovascular diseases including stroke. The Hisayama Study revealed that the risk of stroke in the diabetic patients was twice as high as in the non-diabetic people in a general Japanese population [1,2]. Furthermore, if stroke occurs in diabetic patients, their outcomes may be less favorable than non-diabetic patients. A large number of studies have demonstrated residual neurological deficits and the functional outcome to be worse and consequently the hospital and long-term mortality were worse in diabetic patients [3-5], although a few other studies did not confirm these effects [6-8].

Very few observational studies have assessed the association between the prestroke glycemic control (PSGC) status and clinical outcome in acute stroke patients. A previous study with a small number of subjects suggested that the prestroke blood glucose level was not associated with stroke outcome [9]. However, the impact of the PSGC status on clinical outcome is still unknown because there have been so few such studies conducted.

The aim of the present study was to investigate the association between the PSGC status, defined by hemoglobin (Hb) A1c on admission, and neurological and functional outcomes after acute ischemic stroke.

Subjects and Methods

Study subjects and a Description of the Fukuoka Stroke Registry

The Fukuoka Stroke Registry (FSR) is a multicenter hospital-based registry in which acute stroke patients were enrolled. Kyushu University Hospital and six other stroke centers in Fukuoka, Japan, participated in this registry (see appendix). The study design was approved by the institutional review boards (IRB) of the ethics committee in all hospitals. IRB approved the study protocols and related materials, such as informed consent, document and study brochures, after careful investigation into the protocols and the matters concerning the ethics of the study to protect the rights, safety and welfare of all participants.

The FSR consists of two database systems, i.e. prospective and retrospective databases. In the prospective database, we have been recruiting stroke patients admitted to the participating hospitals within 7 days after onset since June 2007. A total of 3666 cases of stroke were registered as of August 2010. In a prospective database, the patients

participated in the study on voluntary basis after they were fully informed of the objectives and methods of the study, risk to the patients and benefit to the society. They consented to the collection of data from medical records, inquiry concerning medical condition and activities of daily living (ADL) after discharge, and blood samples. Written informed consent was obtained from all patients. This database consists of demographic characteristics, medical history, prehospital, emergency and in-hospital interventions, and patient states including ADL, neurological symptoms and laboratory data during hospitalization. For the retrospective study, we reviewed the medical records of all consecutive patients admitted to the participating hospitals within 24 hours of onset during the period between June 1999 and May 2007, and collected similar information as is included in the prospective database. A total of 5497 cases of stroke were registered in the retrospective database during this period.

Definition of stroke

Stroke was defined as a sudden onset of nonconvulsive and focal neurological deficit persisting for more than 24 hours, and was classified into ischemic stroke, brain hemorrhage, subarachnoid hemorrhage, or other type of stroke by means of brain imaging (computed tomography and/or magnetic resonance imaging). Ischemic stroke was further classified into four subtypes, i.e. lacunar infarction, atherothrombotic infarction, cardioembolic infarction, and unclassified infarction, on the basis of the Classification of Cerebrovascular Disease III proposed by the National Institute of Neurological Disorders and Stroke [10], as well as on the basis of the diagnosis criteria of the Trial of Org 10172 in Acute Stroke Treatment (TOAST) study [11] and the Cerebral Embolism Task Force [12] for ischemic stroke subtypes. Non-cardioembolic infarction was defined either of lacunar, atherothrombotic or unclassified infarction.

Patient selection

Among a total of 9163 cases in the FSR prospective and retrospective databases, 8637 cases were classified as ischemic strokes. After excluding cases with recurrent strokes, impairment of daily living before onset, hospitalization more than 24 hours from onset, and no HbA1c data on admission, 3627 patients were analyzed in the present study (Figure 1).

Clinical assessment

HbA1c was measured according to the Japan Diabetes Society (JDS)/Japan Society of Clinical Chemistry (JSCC) standardization scheme. The values were standardized with national calibrators, the Japanese standard reference materials. The HbA1c values used in the present analysis were obtained by the addition of 0.4% to the JDS/JSCC-based HbA1c values, because the JDS/JSCC-based HbA1c is 0.4% lower than that measured by the National Glycohemoglobin Standardization Program (NGSP) system [13]. The patients were then classified into four groups according to their PSGC status, based on the criteria suggested by the JDS as follows: excellent (HbA1c<6.2%), good (6.2%≤HbA1c<6.9%), fair (6.9%≤HbA1c<8.4%) and poor (HbA1c≥8.4%) [14]. Poststroke casual blood glucose was also measured on admission. A diagnosis of diabetes mellitus was determined by the diagnostic criteria of the JDS [13] in the chronic stage or based on a medical history of diabetes. In patients with known diabetes, the use of oral hypoglycemic agents and insulin were investigated.

Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic pressure ≥90 mmHg in the chronic stage or as current treatment with antihypertensive drugs. Dyslipidemia was defined as either a low-density lipoprotein-cholesterol level ≥3.62 mmol/L, high-density lipoprotein-cholesterol level <1.03 mmol/L, triglycerides ≥1.69 mmol/L or current treatment with a cholesterol-lowering drug. Atrial fibrillation was diagnosed based on electrocardiographic findings on admission or during hospitalization. Smoking was defined as current cigarette smoking and alcohol intake as habitual consumption of alcohol beverages before the onset of stroke.

Blood pressure and body mass index were measured on admission. Thrombolytic therapy was defined as intravenous or intra-arterial administration of thrombolytic agents such as recombinant tissue plasminogen activator and urokinase in the acute phase of the stroke. Infectious complications were defined as any infectious diseases such as pneumonia, urinary tract infection and sepsis during hospitalization.

Study outcomes

The neurological severity was scaled by the National Institutes of Health Stroke Scale (NIHSS) score on admission and at discharge. Neurological improvement was defined as a ≥4 point decrease in the NIHSS during hospitalization or a zero point status on the NIHSS at discharge [15]. Neurological deterioration was defined as a ≥1 point increase in

the NIHSS during hospitalization. In this study, to evaluate the neurological changes during hospitalization, we modified the definition originally reported by Weimar et al. in which neurological worsening was defined as an increase of 1 point or more on NIHSS from hospital admission until 48 to 72 hours later [16]. Death was defined as all-cause mortality during hospitalization. To evaluate the short-term functional outcome, post-stroke functional impairment at discharge was graded using a modified Rankin Scale (mRS). A poor functional outcome was defined as death (mRS of 6) or dependency (mRS of 2 to 5).

Statistical analysis

Statistical analyses were performed using the JMP version 7 software program (SAS Institute Inc., Cary, NC, USA). The clinical characteristics among the PSGC groups were compared by logistic regression analysis, analysis of variance or the Wilcoxon rank sum test. Age- and sex-adjusted or multivariate-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for each study outcome were estimated by logistic regression analysis. The heterogeneity of the PSGC's effects on each outcome between non-cardioembolic and cardioembolic subtypes was tested by adding an interaction term to the relevant multivariate logistic model. P values < 0.05 were considered to be statistically significant.

Results

Demographics of the patients

The mean age of the study subjects was 69±12 years old and 1366 patients (37.7%) were female. The mean value of HbA1c was 6.4±1.5%, and 1233 patients (34.0%) had been diagnosed as having diabetes before onset or were newly diagnosed during hospitalization. A total of 588 patients (16.2%) were administered antidiabetic treatment before the stroke, including oral hypoglycemic agents and insulin. The mean duration of hospitalization was 27±22 days.

Table 1 shows the clinical characteristics of the patients according to their PSGC status. The frequencies of hypertension, dyslipidemia and smoking increased with a poorer PSGC status, although atrial fibrillation was less frequent in those with a poorer PSGC status. The body mass index and blood pressure and casual blood glucose on admission were significantly higher in the patients with a poor PSGC status. Concerning

the stroke subtypes, the proportion of non-cardioembolic infarctions was higher in subjects with the poorer PSGC status. The median (interquartile range) of the NIHSS on admission was 4 (2-8), 4 (2-8), 4 (2-8) and 3.5 (2-6) in patients with excellent, good, fair and poor PSGC, respectively. There was no statistically significant difference in the NIHSS at admission among the PSGC groups (P=0.20, Wilcoxon rank sum test).

Association between PSGC status and neurological outcomes

Table 2 shows the association between the PSGC status and each study outcome. The age- and sex-adjusted ORs for neurological improvement decreased substantially as the PSGC status became poorer. In contrast, the signs of neurological deterioration increased with poorer PSGC status. These findings were still observed after adjustment for possible confounding factors such as age, sex, baseline NIHSS, stroke subtype, systolic blood pressure, hypertension, dyslipidemia, atrial fibrillation, body mass index, thrombolytic therapy and infectious complications (model 1, all p values for trends were <0.001). In this model, the probability of achieving a neurological improvement was significantly lower, and the risk of a neurological deterioration was significantly higher in both the fair and poor PSGC groups than in the excellent PSGC group. Similar trends were still observed when the admission blood glucose levels were additionally included (model 2, all p values for trend were <0.002). The frequency of death during hospitalization was not different among the PSGC groups.

We then further analyzed the association between the PSGC status and each outcome separately for non-cardioembolic and cardioembolic infarctions. As shown in Figure 2, the multivariate-adjusted ORs for neurological improvement significantly decreased with a poorer PSGC status in patients with non-cardioembolic infarctions (p for the trend <0.001). A similar pattern was observed in patients with cardioembolic infarctions, but it did not reach the level of significance, probably due to the limited sample size (p for the trend = 0.29). In any case, there was no evidence of heterogeneity between the ORs in non-cardioembolic and in cardioembolic subtypes (p for heterogeneity = 0.29). As shown in Figure 3, the risks of neurological deterioration significantly increased with poorer PSGC status in both subtypes, and no evidence of heterogeneity between the subtypes was found (p for heterogeneity = 0.93).

Association between the PSGC status and short-term functional outcomes

The risks of a poor functional outcome were higher in the patients with poorer PSGC status in all logistic models (Table 2, all p values for the trend <0.001). In both the age- and sex-adjusted and multivariate model 1, the risk of a poor functional outcome was significantly higher in both the fair and poor PSGC groups than in the excellent PSGC group. However, the fair PSGC group failed to show a significant association with the functional outcome in the multivariate model 2. As shown in Figure 4, the risk of poor functional outcome significantly increased with poorer PSGC status in patients with non-cardioembolic infarctions (p for the trend = 0.001). A similar but nonsignificant association was observed in patients with cardioembolic infarctions (p for the trend = 0.15), and there was no evidence of heterogeneity between the subtypes (p for heterogeneity = 0.55).

Discussion

It remains to be fully elucidated whether the PSGC status affects the clinical course of ischemic stroke. A previous study with 99 ischemic stroke patients suggested that the prestroke blood glucose level did not have any predictive value for stroke outcome [9]. However, the present study has shown that poor glycemic control before stroke occurrence may be detrimental to the clinical course after onset, and consequently lead to a poor functional outcome of ischemic stroke.

Since non-cardioembolic infarction is mainly caused by atherosclerosis, and diabetes is a major risk factor for atherosclerosis, the effects of the PSGC status on clinical outcomes might differ among stroke subtypes. However, we found no evidence of heterogeneity between the ORs for each outcome in the non-cardioembolic and cardioembolic subtypes. Therefore, the PSGC status has similar effects on the clinical course and short-term outcome, regardless of stroke subtype.

The mechanism by which poor glycemic control before onset is associated with an unfavorable outcome of ischemic stroke is unclear. There are some possible hypotheses regarding the association between the PSGC status and outcome. Many studies have shown that hyperglycemia after stroke onset has adverse effects on the clinical course of ischemic stroke [17-23], although some other studies did not acknowledge this effect [6-8]. Baird et al. reported that persistent hyperglycemia was associated with the expansion of infarct volume and worse functional outcome [21]. Poppe et al found that admission hyperglycemia was independently associated with outcome both in patients

with and without diabetes [24]. Hyperglycemia itself probably results in neurotoxicity and induces a procoagulant state [25]. In this study, the initial NIHSS was similar among the four PSGC groups defined by admission HbA1c. However, PSGC was found to be an independently significant predictor of the neurological and clinical outcomes in the multivariate model 1, and this relationship remained significant even after adjusting for blood glucose levels in multivariate model 2. Because the HbA1c level at admission, which is considered to be an index of glucose control during the past few months before stroke onset, showed a positive correlation with casual blood glucose level at admission, it may be possible that prestroke and poststroke hyperglycemia contributed to an exacerbation of the clinical course, and a poorer short-term outcome in the patients with a poor PSGC status.

Other factors could also be involved in the mechanism(s). Blood pressure was significantly higher in patients with poor glycemic control. The acute blood pressure level is associated with neurological deterioration in patients with ischemic stroke [26]. Therefore, high blood pressure may also be associated with the poor outcome in patients with a poor PSGC status. Although various factors may also be involved, the PSGC status had a significant impact on the short-term outcome even after adjustment for possible confounding factors including stroke subtypes, admission blood glucose and admission blood pressure. These results indicate that PSGC is an independent predictor for a poor clinical outcome in patients with ischemic stroke.

Recent randomized controlled trials have revealed that intensive glycemic control could not reduce the cardiovascular risk in diabetic patients (median glycated hemoglobin levels 6.4% (ACCORD [27]) and 6.9% (VADT [28]), mean glycated hemoglobin level 6.5% (ADVANCE [29])) compared with conventional control. From this point of view, less intense therapy may be recommended for high-risk diabetic patients, especially elderly patients, to avoid adverse events such as hypoglycemia. Before intensifying the therapy regimen, the patient's life expectancy, risk of hypoglycemia and the presence of cardiovascular diseases should be considered [30].

It is plausible that the poststroke blood glucose is higher in patients with poor PSGC, whereas it is better controlled in patients with better PSGC status. We did not verify whether prestroke intensive treatment of blood glucose affects the clinical outcome after ischemic stroke. However, if poststroke hyperglycemia is detrimental to the clinical outcome in ischemic stroke, a better PSGC status may be beneficial. Further studies are

needed to elucidate whether treatment to provide better glycemic control before onset improves the clinical course and outcome in patients with ischemic stroke.

The present study had several strengths. The number of subjects was large, and they were recruited from multiple stroke care centers which treat patients with standardized criteria. In addition, possible confounding factors were extensively collected in all subjects and adjusted in multivariate analysis. However, there were also limitations to this study. There was a selection bias in this study, since 1006 patients without HbA1c measurement data on admission were excluded from the present analyses. The proportion of diabetic subjects was smaller among the excluded patients (16.3%) than the patients included in the study (34.0%). Therefore, we consider that the ORs shown in the patient analyses might thus have been underestimated, but this selection bias did not affect the study conclusions. Although we adjusted for the blood glucose levels on admission as a confounding factor in the multivariate model 2, the changes in the blood glucose level and its management during hospitalization were not considered in the analyses. Since it was an observational study, and therefore unable to control treatment, the efficacy of treatment for blood glucose and the optimal range for glycemic control remain unclear. Moreover, the ORs for cardioembolic infarction did not reach statistically significant levels, probably due to the small sample size. Further studies will be required to elucidate whether control of prestroke blood glucose improves the clinical outcome after ischemic stroke.

Conclusion

In conclusion, a higher HbA1c at onset was found to be associated with an unfavorable clinical outcome of ischemic stroke. In comparison to an excellent PSGC, a fair or poor PSGC was associated with unfavorable neurological outcomes and a poor PSGC was found to be related to a poorer functional outcome, while no association was observed between the PSGC status and death during hospitalization. In high-risk diabetic patients, glycemic control should be reappraised from the standpoint of functional outcome after ischemic stroke.

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Conflict of interests: None

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Figure Legends

Figure 1. Flow chart of patient selection.

Figure 2. Multivariate-adjusted ORs and 95% CIs for neurological improvement in subjects with non-cardioembolic (closed squares) and cardioembolic (open squares) infarctions according to their PSGC status. The multivariate model included age, sex, baseline NIHSS in quartiles, systolic blood pressure on admission, casual blood glucose on admission, hypertension, dyslipidemia, atrial fibrillation, BMI, thrombolytic therapy and infectious complications. The abscissa is shown on a logarithmic scale.

Figure 3. Multivariate-adjusted ORs and 95% CIs for neurological deterioration in subjects with non-cardioembolic (closed squares) and cardioembolic (open squares) infarctions according to their PSGC status. The multivariate model included age, sex, baseline NIHSS in quartiles, systolic blood pressure on admission, casual blood glucose on admission, hypertension, dyslipidemia, atrial fibrillation, BMI, thrombolytic therapy and infectious complications. The abscissa is shown on a logarithmic scale.

Figure 4. Multivariate-adjusted ORs and 95% CIs for functional outcome (death or dependency) in subjects with non-cardioembolic (closed squares) and cardioembolic (open squares) infarctions according to the PSGC status. The multivariate model included age, sex, baseline NIHSS in quartiles, systolic blood pressure on admission, casual blood glucose on admission, hypertension, dyslipidemia, atrial fibrillation, BMI, thrombolytic therapy and infectious complications. The abscissa is shown on a logarithmic scale.

Table 1. Clinical background of the patients according to PSGC status

	PSGC status (range of HbA1c)				*P* for trend
	Excellent (<6.2%) (n=2251)	Good (6.2-6.8%) (n=542)	Fair (6.9-8.3%) (n=470)	Poor (≥8.4%) (n=364)	
Age, y	70±13	71±10*	70±10	66±10*	<0.001
Female, n (%)	889 (39.5%)	199 (36.7%)	154 (32.8%)*	124 (34.1%)*	0.003
Risk factors					
Hypertension, n (%)	1595 (70.9%)	431 (79.5%)*	393 (83.6%)*	264 (72.5%)	<0.001
Diabetes, n (%)	181 (14.7%)	257 (47.4%)*	439 (93.4%)*	356 (97.8%)*	<0.001
Use of oral hypoglycemic agents or insulin, n (%)	50 (2.2%)	99 (18.3%)*	265 (56.4%)*	174 (47.8%)*	<0.001
Dyslipidemia, n (%)	764 (33.9%)	257 (47.4%)*	213 (45.3%)*	190 (52.2%)*	<0.001
Atrial fibrillation, n (%)	605 (26.9%)	145 (26.8%)	99 (21.1%)*	58 (15.9%)*	<0.001
Smoking, n (%)	1036 (46.0%)	259 (47.8%)	228 (48.5%)	189 (51.9%)*	0.03
Alcohol intake, n (%)	899 (39.9%)	211 (38.9%)	168 (35.7%)	151 (41.5%)	0.64
Physical and laboratory data on admission					
Body Mass Index	22.8±3.5	23.8±3.7*	23.9±3.7*	24.2±3.6*	<0.001
Systolic blood pressure (mmHg)	161±30	163±29	165±29*	169±31*	<0.001
Diastolic blood pressure (mmHg)	88±18	87±18	88±17	92±18*	0.006
Casual blood glucose (mmol/L)	6.8±1.9	7.9±2.3*	10.4±3.3*	14.4±5.0*	<0.001
Stroke subtype					
Non-cardioembolic, n (%)	1616 (71.8%)	377 (69.6%)	363 (77.2%)	304 (83.5%)	<0.001
Atherothrombotic, n (%)	451 (20.0%)	121 (22.3%)	119 (25.3%)	106 (29.1%)	
Lacunar, n (%)	575 (25.5%)	149 (27.5%)	140 (29.8%)	134 (36.8%)	
Unclassified, n (%)	590 (26.2%)	107 (19.7%)	104 (22.1%)	64 (17.6%)	
Cardioembolic, n (%)	635 (28.2%)	165 (30.4%)	107 (22.8%)	60 (16.5%)	

The values are expressed as the means ± SD or number of subjects (percentage). *P<0.05 vs. Excellent group.

Table 2. Odds ratios for clinical outcome according to PSGC status

		Age- and sex-adjusted			Multivariate-adjusted (Model 1)			Multivariate-adjusted (Model 2)		
	Number of events	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Neurological improvement										
Excellent PSGC	1166/2251 (51.8%)	1.00	reference	0.54	1.00	reference		1.00	reference	
Good PSGC	271/542 (50.0%)	0.94	(0.78-1.14)	0.001	0.84	(0.68-1.04)	0.12	0.84	(0.67-1.04)	0.11
Fair PSGC	204/470 (43.4%)	0.72	(0.59-0.88)	<0.001	0.77	(0.61-0.97)	0.03	0.76	(0.59-0.98)	0.04
Poor PSGC	136/364 (37.4%)	0.53	(0.42-0.67)	<0.001	0.52	(0.40-0.68)	<0.001	0.50	(0.36-0.71)	<0.001
P for the trend				0.54			<0.001			<0.001
Neurological deterioration										
Excellent PSGC	218/2251 (9.7%)	1.00	reference		1.00	reference		1.00	reference	
Good PSGC	59/542 (10.9%)	1.12	(0.82-1.52)	0.46	1.01	(0.69-1.45)	0.95	1.02	(0.70-1.46)	0.93
Fair PSGC	71/470 (15.1%)	1.70	(1.27-2.27)	<0.001	1.71	(1.19-2.41)	0.004	1.66	(1.12-2.43)	0.01
Poor PSGC	57/364 (15.7%)	2.04	(1.47-2.79)	<0.001	2.37	(1.62-3.43)	<0.001	2.32	(1.39-3.83)	0.001
P for the trend				<0.001			<0.001			0.001
Death										
Excellent PSGC	72/2251 (3.2%)	1.00	reference		1.00	reference		1.00	reference	
Good PSGC	12/542 (2.2%)	1.49	(0.83-2.90)	0.19	1.24	(0.63-2.69)	0.55	1.20	(0.60-2.64)	0.61
Fair PSGC	17/470 (3.6%)	0.86	(0.51-1.52)	0.59	1.04	(0.50-2.37)	0.92	1.02	(0.46-2.45)	0.97
Poor PSGC	13/364 (3.6%)	0.72	(0.40-1.38)	0.30	0.48	(0.22-1.13)	0.09	0.46	(0.16-1.38)	0.16
P for the trend				0.38			0.28			0.46
Poor functional outcome (Death or dependency)										
Excellent PSGC	1025/2251 (45.5%)	1.00	reference		1.00	reference		1.00	reference	
Good PSGC	266/542 (49.1%)	1.12	(0.92-1.36)	0.26	1.20	(0.93-1.56)	0.16	1.16	(0.90-1.51)	0.25
Fair PSGC	246/470 (52.3%)	1.35	(1.10-1.66)	0.004	1.34	(1.02-1.77)	0.04	1.26	(0.94-1.71)	0.12
Poor PSGC	202/364 (55.5%)	1.84	(1.46-2.32)	<0.001	2.52	(1.88-3.39)	<0.001	2.30	(1.56-3.40)	<0.001
P for the trend				<0.001			<0.001			<0.001

OR: odds ratio, CI: confidence interval, the multivariate model 1 included age, sex, baseline NIHSS in quartiles, stroke subtype (non-cardioembolic or cardioembolic), systolic blood pressure on admission, hypertension, dyslipidemia, atrial fibrillation, BMI, thrombolytic therapy and infectious complications. The multivariate model 2 included the same variables in the model 1 and casual blood glucose on admission.

Appendix

FSR Investigators

The participating Hospitals in the FSR were as follows: Kyushu University Hospital, National Hospital Organization Kyushu Medical Center, National Hospital Organization Fukuoka Higashi Medical Center, Fukuoka Red Cross Hospital, St. Mary's Hospital, Nippon Steel Yawata Memorial Hospital, Japan Labour Health and Welfare Organization Kyushu Rosai Hospital.

The Steering Committee included: Takao Ishitsuka, MD; Shigeru Fujimoto, MD: Department of Cerebrovascular Disease, Nippon Steel Yawata Memorial Hospital. Setsuro Ibayashi, MD; Kenji Kusuda, MD: Department of Medicine, Seiai Rehabilitation Hospital. Shuji Arakawa, MD: Department of Cerebrovascular Disease, Japan Labour Health and Welfare Organization Kyushu Rosai Hospital. Kinya Tamaki, MD; Katsumi Irie, MD: Department of Cerebrovascular Disease, Hakujyuji Hospital. Kenichiro Fujii, MD: Department of Cerebrovascular Disease, Fukuoka Red Cross Hospital. Yasushi Okada, MD; Masahiro Yasaka, MD: Department of Cerebrovascular Disease and Clinical Research Institute, National Hospital Organization Kyushu Medical Center. Tetsuhiko Nagao, MD: Department of Medicine, Haradoi Hospital. Hiroaki Ooboshi, MD: Department of Internal Medicine, Fukuoka Dental Collage Medical and Dental Hospital. Tsuyoshi Omae, MD: Department of Medicine, Imazu Red Cross Hospital. Kazunori Toyoda, MD: Department of Cerebrovascular Disease, National Cardiovascular Center. Hiroshi Nakane, MD: Cerebrovascular Division, Department of Medicine, National Hospital Organization Fukuoka-Higashi Medical Center. Kenji Fukuda, MD: Department of Cerebrovascular Disease, St. Mary's Hospital. Seizo Sadoshima, MD: Yoshizuka Hayashi Hospital.

The Research Working Group included: Yuka Kanazawa, Tomohiro Yubi, Yuichi Miyazaki, Ryu Matsuo, Junichi Takada, Shoji Arihiro, Kazuhiro Kishikawa: Department of Medicine and Clinical Science, Graduate School of Medical Sciences, Kyushu University.

Figure1

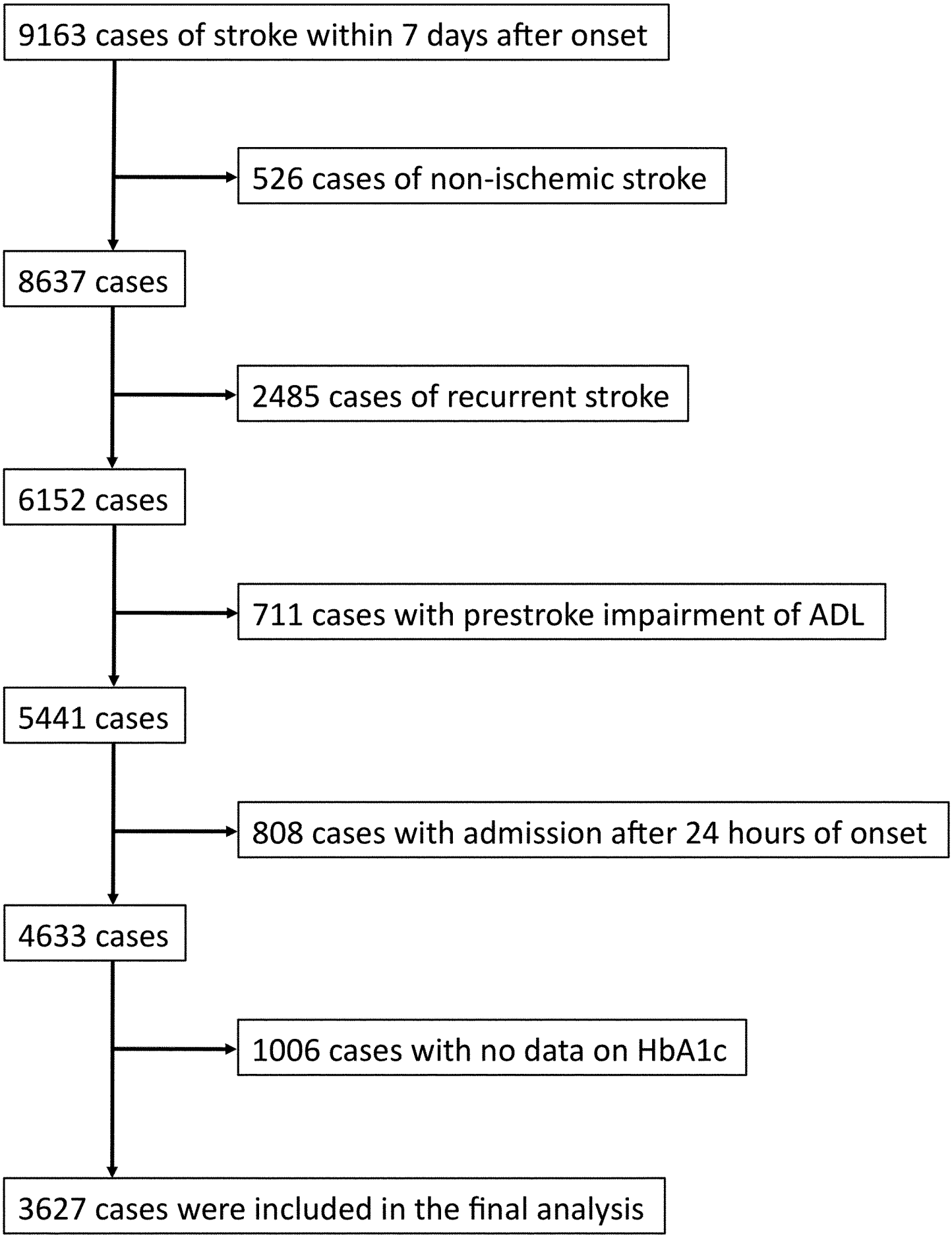

9163 cases of stroke within 7 days after onset
526 cases of non-ischemic stroke
8637 cases
2485 cases of recurrent stroke
6152 cases
711 cases with prestroke impairment of ADL
5441 cases
808 cases with admission after 24 hours of onset
4633 cases
1006 cases with no data on HbA1c
3627 cases were included in the final analysis

Figure2

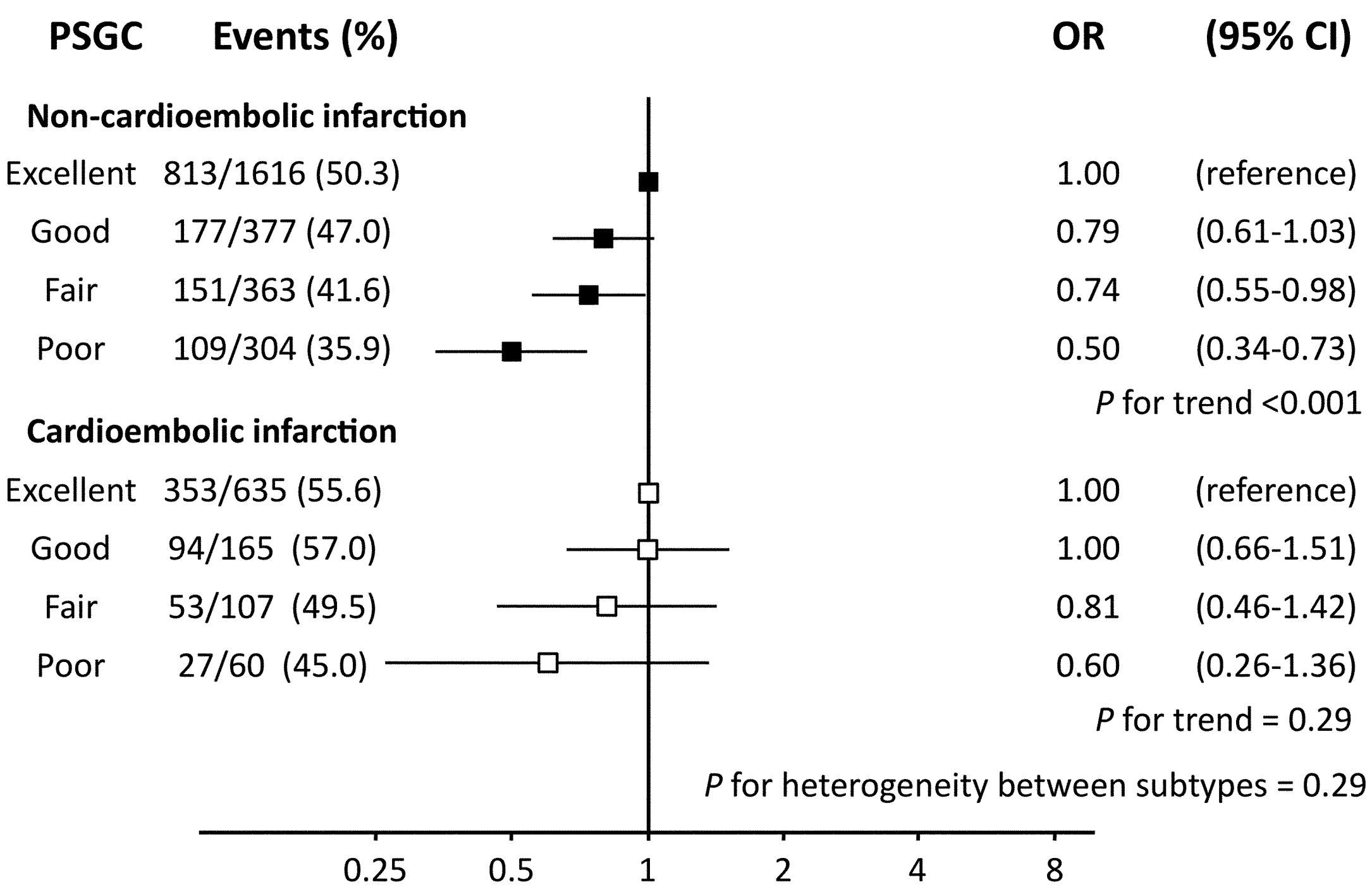

PSGC
Events (%)
OR
(95% CI)
Non-cardioembolic infarction
Excellent 813/1616 (50.3)
1.00 (reference)
Good 177/377 (47.0)
0.79 (0.61-1.03)
Fair 151/363 (41.6)
0.74 (0.55-0.98)
Poor 109/304 (35.9)
0.50 (0.34-0.73)
P for trend <0.001
Cardioembolic infarction
Excellent 353/635 (55.6)
1.00 (reference)
Good 94/165 (57.0)
1.00 (0.66-1.51)
Fair 53/107 (49.5)
0.81 (0.46-1.42)
Poor 27/60 (45.0)
0.60 (0.26-1.36)
P for trend = 0.29
P for heterogeneity between subtypes = 0.29
0.25
0.5
1
2
4
8

Figure3

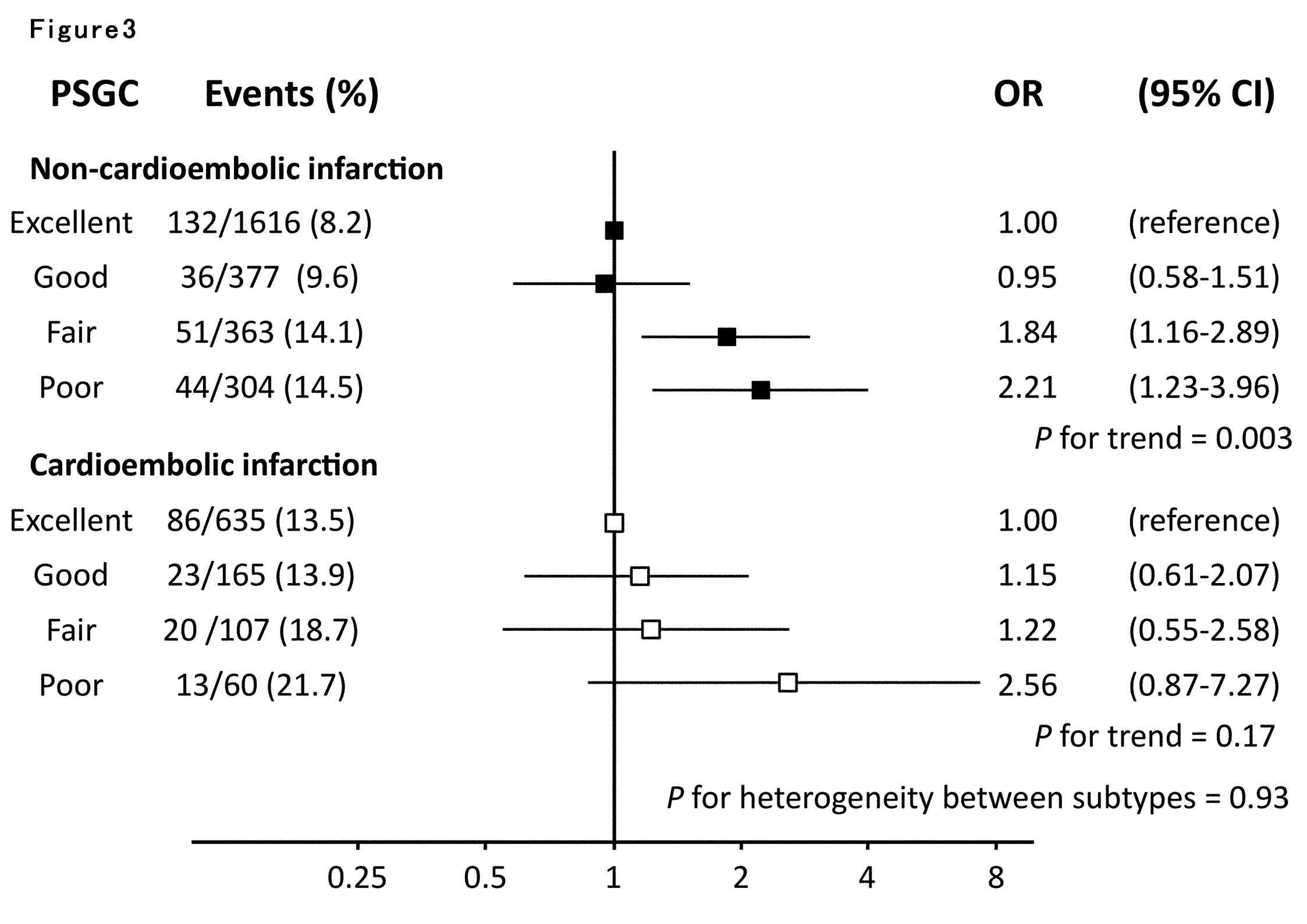
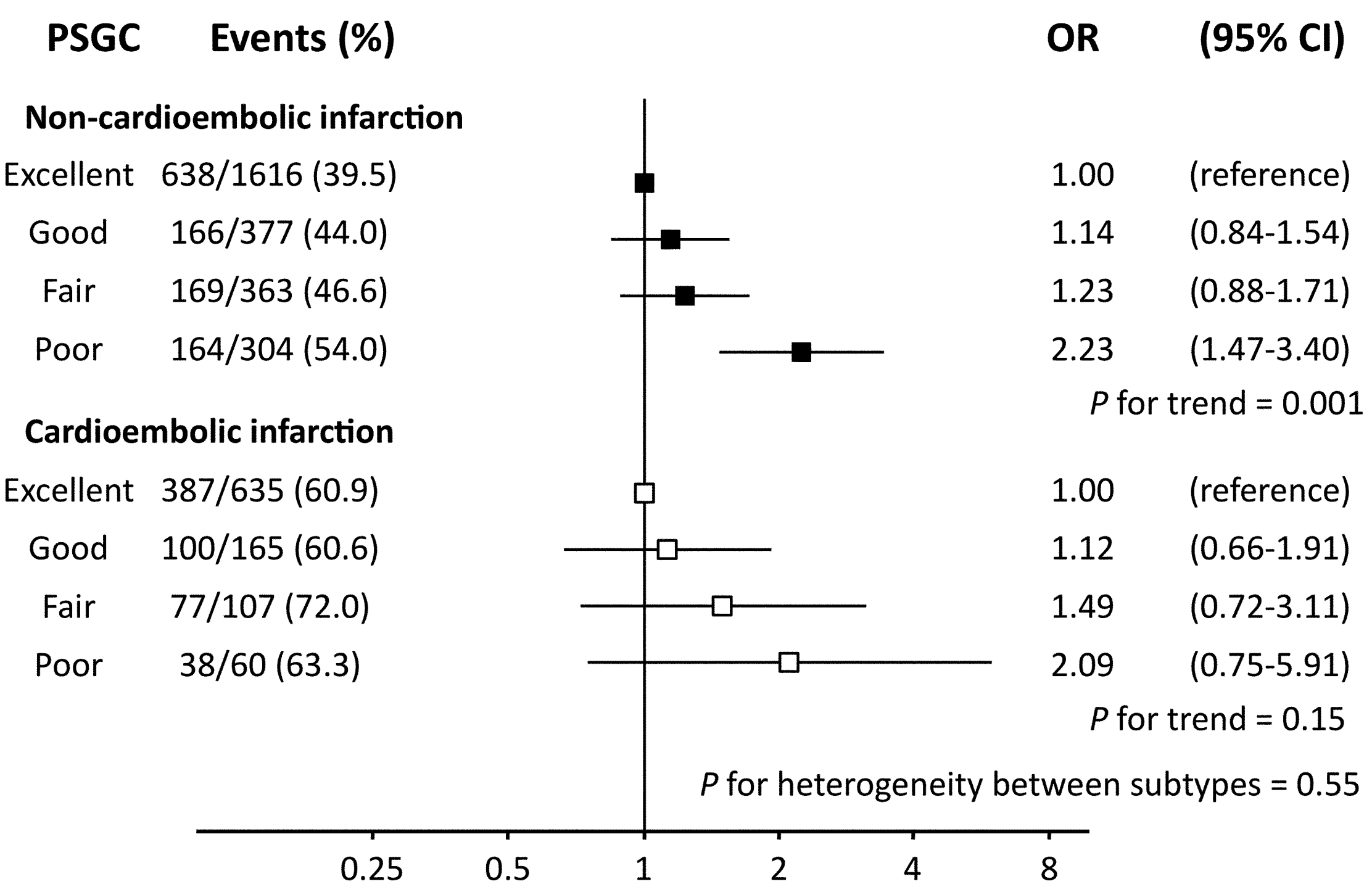

PSGC
Events (%)
OR
(95% CI)
Non-cardioembolic infarction
Excellent 132/1616 (8.2)
1.00 (reference)
Good 36/377 (9.6)
0.95 (0.58-1.51)
Fair 51/363 (14.1)
1.84 (1.16-2.89)
Poor 44/304 (14.5)
2.21 (1.23-3.96)
P for trend = 0.003
Cardioembolic infarction
Excellent 86/635 (13.5)
1.00 (reference)
Good 23/165 (13.9)
1.15 (0.61-2.07)
Fair 20 /107 (18.7)
1.22 (0.55-2.58)
Poor 13/60 (21.7)
2.56 (0.87-7.27)
P for trend = 0.17
P for heterogeneity between subtypes = 0.93
0.25
0.5
1
2
4
8

Figure4


PSGC
Events (%)
OR
(95% CI)
Non-cardioembolic infarction
Excellent 638/1616 (39.5)
1.00 (reference)
Good 166/377 (44.0)
1.14 (0.84-1.54)
Fair 169/363 (46.6)
1.23 (0.88-1.71)
Poor 164/304 (54.0)
2.23 (1.47-3.40)
P for trend = 0.001
Cardioembolic infarction
Excellent 387/635 (60.9)
1.00 (reference)
Good 100/165 (60.6)
1.12 (0.66-1.91)
Fair 77/107 (72.0)
1.49 (0.72-3.11)
Poor 38/60 (63.3)
2.09 (0.75-5.91)
P for trend = 0.15
P for heterogeneity between subtypes = 0.55
0.25
0.5
1
2
4
8