Primary coronary intervention for ST-elevation myocardial infarction in Indonesia and the Netherlands: a comparison

Y.B. Juwana, J. Wirianta, J.P. Ottervanger, J.-H.E. Dambrink, A.W.J. van 't Hof, A.T.M. Gosselink, J.C.A. Hoorntje, M.-J. de Boer, H. Suryapranata

Background. Although the beneficial effects of primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) have been demonstrated in a number of trials, most studies were conducted in Western countries. Experience, logistics and patient characteristics may differ in other parts of the world.

Methods. Consecutive patients treated with primary PCI in Cinere Hospital, Jakarta, Indonesia, between January 2008 and October 2008 were compared with those treated in the Isala Clinics, Zwolle, the Netherlands.

Results. During the study period, a total of 596 patients were treated by primary PCI, 568 in Zwolle and 28 in Jakarta. Patients in Indonesia were younger (54 vs 63 years), more often had diabetes (36 vs. 12%) and high lipids and were more often smokers (68 vs. 31%). Time delay between symptom onset and admission was longer in Indonesia. Patients from Indonesia more often had signs of heart failure at admission. The time between admission and balloon inflation was longer in Indonesia. At angiography, patients from Indonesia more often had multivessel disease. There was no difference in the percentage of restoration of TIMI 3 flow by primary PCI between the two hospitals.

Conclusion. Patients with STEMI in Indonesia have a higher risk profile compared with those in the Netherlands, according to prevalence of coronary risk factors, signs of heart failure, multivessel disease and patient delay. Time delay between admission and balloon inflation was much longer in Indonesia, because of both logistic and financial reasons. (Neth Heart J 2009;17:418-21.)

Keywords: developing countries, Asia, infarction

The most important therapeutic goal in the treatment of patients with ST-elevation myocardial infarction (STEMI) is achievement of early and complete reperfusion of the infarct-related vessel. Effective reperfusion can be achieved by either fibrinolytic therapy or primary percutaneous coronary intervention (PCI) without antecedent fibrinolysis. A total of 23 randomised controlled trials, involving more than 7500 patients, have demonstrated the superiority of primary PCI over fibrinolytic therapy,¹ with the absolute mortality advantage of primary PCI greatest in high-risk patients such as those with cardiogenic shock.^{2,3} However, almost all these trials were performed in the United States or Western Europe. The situation and the efficacy of primary PCI may differ in other parts of the world, with regards to logistics, experience of PCI centres and patient characteristics. More insights into potential differences between these regions and the Western world are important to estimate whether primary PCI will also be effective in these countries.

It is expected that cardiovascular mortality will increase in the South-East Asian region.⁴ Also in Indonesia, both morbidity and mortality due to coronary artery disease is high. This may be caused by a high prevalence of diabetes,⁵ hypertension⁶ and smoking.^{7,8} In a developing country such as Indonesia, probably only a minority of patients with STEMI are treated with primary PCI. But procedures as well as patients who are treated with primary PCI may also differ from the Western world. To compare treatment

Y.B. Juwana

J. Wirianta

Department of Cardiology, Cinere Hospital, Jakarta, Indonesia

J.P. Ottervanger

J.-H.E. Dambrink

A.W.J. van 't Hof

A.T.M. Gosselink

J.C.A. Hoorntje

M.-J. de Boer

H. Suryapranata

Department of Cardiology, Isala Clinics, Zwolle, the Netherlands

Correspondence to: J.P. Ottervanger

Department of Cardiology, Isala Clinics, PO Box 10500,
8000 GM Zwolle, the Netherlands

E-mail v.r.c.derks@isala.nl

with primary PCI in Europe (the Netherlands) and Indonesia, we performed a prospective registry in two hospitals.

Patients and methods

All consecutive patients treated with primary PCI for STEMI in either Cinere Hospital, Jakarta, Indonesia or the Isala Clinics, Zwolle, the Netherlands between January and October 2008 were registered in a dedicated database. The Isala Clinics, Zwolle is a hospital with a long experience with primary PCI. Cinere Hospital, Jakarta started performing PCI in 2006, but has a close collaboration with the Isala Clinics and there are always an experienced consultant cardiologist and nursing staff from Zwolle working in Jakarta.

There was no industry involvement in the design, conduct or analysis of the study.

All patients with STEMI, presenting within six hours after symptom onset, or those presenting between six and 24 hours if they had persisting chest pain associated with clinical evidence of on-going ischaemia, were considered eligible for primary PCI and inclusion in the registry.

All patients were pretreated with aspirin, a loading dose of clopidogrel and intravenous nitroglycerin and heparin. Treatment with glycoprotein IIB/IIIA inhibitors was left to the discretion of the physicians. Stenting of the target lesion was performed using standard interventional techniques. After the primary PCI all patients were treated with medication according to the guidelines, including statins and β -blockers. All patients received clopidogrel for at least six months.

Statistical analysis

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 15.0. Continuous data were expressed as mean $\pm$ standard deviation and categorical data as percentages, unless otherwise denoted. Differences between continuous data were performed by Student's *t* test and the χ^2 or Fisher's exact test were used as appropriate for dichotomous data. For all analyses, statistical significance was assumed when the two-tailed probability value was <0.05 .

Results

Data were collected in 596 consecutive patients. The mean age was 62.5 years (range 28 to 96) and 75% were male. The mean time between onset of chest pain and admission was 225 (± 215) minutes. Females were older, 66.2 (± 13.1) years compared with males, 61.2 (± 12.6). The time between symptom onset and admission was comparable in females (230 $\pm$ 217 minutes) and males (223 $\pm$ 214 minutes). During the study period, a total of 568 patients in Zwolle and 28 patients in Cinere Hospital were treated with primary PCI for STEMI. Baseline characteristics of the patients are listed in table 1. Patients from Indonesia were younger, with a trend to more males. The prevalence of diabetes, high lipids and smoking was higher in Indonesian patients. Time between symptom onset and hospital admission was longer in Indonesian patients. In table 2 angiographic measurements are summarised. Time from hospital admission to balloon inflation was much longer in Indonesia. Furthermore, more patients from Indonesia had multivessel disease. The other angiographic characteristics were not different between

Table 1. Differences between patients treated with primary PCI for STEMI in Cinere Hospital, Jakarta and Isala Clinics, Zwolle.

	Isala Clinics, Zwolle (n=568)	Cinere Hospital, Jakarta (n=28)	P value
Age (years)	62.9 $\pm$ 12.8	53.8 $\pm$ 11.6	0.001
Male	75	86	0.19
Diabetes	12	36	0.001
Family history of heart disease	37	32	0.64
High lipids	19	46	0.001
Hypertension	42	46	0.65
Smoking	31	68	0.01
Previous MI	11	18	0.27
Anterior location	39	54	0.13
Killip ≥ 2 on admission	8	52	0.001
Time between onset chest pain and admission (min)	214 $\pm$ 202	413 $\pm$ 325	0.001
SBP on admission (mmHg)	133 $\pm$ 26	117 $\pm$ 23	0.002
DBP admission (mmHg)	81 $\pm$ 17	76 $\pm$ 14	0.12
Heart rate on admission (beats/min)	76.8 $\pm$ 19.6	83.4 $\pm$ 27.3	0.09

SBP=systolic blood pressure, DBP=diastolic blood pressure. Data are given as percentages or mean $\pm$ SD.

Table 2. Angiographic findings in patients treated with primary PCI for STEMI in Cinere Hospital, Jakarta or Isala Clinics, Zwolle.

	Isala Clinics, Zwolle (n=568)	Cinere Hospital, Jakarta (n=28)	P value
Time between admission and balloon inflation (min)	49±33	189±127	0.001
Multivessel disease	51	75	0.01
Infarct-related vessel			
- LAD	39	46	0.40
- RCA	39	39	0.99
TIMI 0 before PCI	59	68	0.34
Stenting	73	71	0.82
Only one stent used	80	75	0.62
TIMI 3 flow after PCI	93	85	0.15

LAD=left anterior descending artery, RCA=right coronary artery, PCI=percutaneous coronary intervention. Data are given as percentages or mean ± SD.

patients from the Netherlands and Indonesia. Death within 30 days after admission was observed in 24 patients in the Netherlands (4.2%) and in one patient (3.6%) in Indonesia (NS).

Discussion

We found important differences between patients treated with primary PCI for STEMI in Indonesia and the Netherlands. Patients in Indonesia had a higher risk profile compared with the Netherlands, with regards to prevalence of coronary risk factors, signs of heart failure and patient delay. Although primary PCI was effective in restoration of TIMI 3 flow in both countries, time delay between admission and balloon inflation was longer in Indonesia.

Clinical implications

Our results suggest that many factors can be improved to reduce morbidity and mortality due to STEMI in Indonesia. First, both health care professionals and politicians should still focus on primary prevention. The high prevalence of unfavourable risk factors in our Indonesian patients was also previously observed in the Indonesian general population.⁹ Patients from Indonesia had a twofold prevalence of smoking in our study. The prevalence of smoking is still high in Indonesia, although there have been campaigns against smoking, particularly because it has been shown that there are no ethnic differences in the benefits of quitting smoking.¹⁰ The Indonesian Ministry of Health already makes use of traditional media such as the wayang kulit (shadow puppet theatre) and warnings about the harmful effects of (passive) smoking. Also the Indonesian Heart Foundation and several foundations, such as the Foundation's No-Smoking Leaders Group (Lembaga Menanggulangi Masalah Merokok, known as Lembaga M3) and the Wanita Indonesia Tanpa Tembakau (WITT) or Indonesian Women Without Tobacco, are fighting against smoking. Even more aggressive public health efforts to limit tobacco use are

now probably urgently needed in Indonesia. Also, the prevalence of diabetes was high in our study. This may be related to a high prevalence of diabetes in the general population in Indonesia, which may in part be associated with the metabolic syndrome. Studies of people living in rural areas of East Java and Bali show an increasing prevalence of 1.5% in 1982 to 5.7% in 1995 among the urban population. Comparative studies indicate that metabolic responses to obesity may be greater in South and East Asians than their Western counterparts at given body mass indexes.^{11,12} It was previously suggested that early detection of asymptomatic diabetes in Indonesia should be encouraged, either at the hospital or the doctor's private office.¹³ Furthermore, it has been demonstrated that the management of type 2 diabetes in the Western Pacific region varies widely, where hypertension and microalbuminuria are often untreated.¹⁴

A second important goal in the treatment of patients with STEMI in Indonesia should be to reduce the time between symptom onset and first balloon inflation. There is a strong association between time delay and mortality in patients with STEMI treated by primary PCI.¹⁵ This can be separated into delay between symptom onset and hospital admission and in delay between admission and balloon inflation. There can be several strategies to decrease time delays.¹⁶ All steps should be considered for improvement, including the patient's ability to recognise their symptoms and to promptly contact the medical system, the time necessary to transport the patient to the hospital, the decision process on arrival, and the requisite time to implement the reperfusion strategy. Possibly, in Indonesia particularly ambulance transport systems can be improved, with regional approaches round hospitals with PCI facilities and prehospital ECGs transmitted to an emergency department or relying on ambulance-based paramedics trained to diagnose STEMI and to determine which patients should be transported directly to specialised PCI centres.¹⁷

More importantly, in Indonesia much delay and even the impossibility to offer primary PCI to patients with STEMI may be influenced by financial considerations. About 80% of the Indonesian population has no health insurance coverage. Although the insurance scheme for civil servants (Askes) may have had a strongly positive impact on access of poor patients to medical care,¹⁸ access to especially all hospital services is still low for the middle- and low-income patients.¹⁹ This problem is difficult to solve in the short term, but should be an effort of government, insurance companies, medical professionals and aid from the Western world. It should be kept in mind that the costs of primary PCI, particularly if performed with 'stand-alone' balloon angioplasty, may be lower than conservative treatment or thrombolysis.²⁰

Limitations

We only studied patients in two hospitals. Particularly in Indonesia, a very large country, the results may have been different in other regions or hospitals. Geographical variation may be of importance, due to differences in ethnics, race, culture and lifestyle. Moreover, we only included a few patients from Indonesia, and we could not therefore perform subgroup analyses. Finally and maybe most importantly, health economics differ greatly between Indonesia and the Netherlands. This may have introduced confounding factors that cannot be detected by this survey. Because of this selection bias, we are now scheduling a larger, prospective registry, with also patients from the University Hospital in Jakarta. However, also then financial reasons may still cause (additional) selection bias, since only selected patients with myocardial infarction are admitted to a hospital, and of those only the happy few may be treated by primary PCI.

Conclusions

Patients with STEMI in Indonesia have a higher risk profile compared with the Netherlands, according to prevalence of coronary risk factors, signs of heart failure and patient delay. Although primary PCI was effective in both countries with regard to restoring TIMI 3 flow, time delay between admission and balloon inflation was longer in Indonesia. Treatment of STEMI can be improved in Indonesia and this should be a combined effort of both government and health care professionals. ■

References

- 1 Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet*. 2003;361:13-20.
- 2 Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. *N Engl J Med*. 1999;341:625-34.
- 3 Zahn R, Schiele R, Schneider S, Gitt AK, Wienbergen H, Seidl K, et al. Primary angioplasty versus intravenous thrombolysis in acute myocardial infarction: can we define subgroups of patients benefiting most from primary angioplasty? *J Am Coll Cardiol*. 2001;37:1827-35.
- 4 Gupta M, Singh N, Verma S. South Asian and cardiovascular risk, what clinicians should know. *Circulation*. 2006;113:e924-9.
- 5 Santoso T. Prevention of cardiovascular disease in diabetes mellitus: by stressing the CARDS study. *Acta Med Indones*. 2006;38:97-102.
- 6 Martiniuk AL, Lee CM, Lawes CM, Ueshima H, Suh I, Lam TH, et al; Asia-Pacific Cohort Studies Collaboration. Hypertension: its prevalence and population-attributable fraction for mortality from cardiovascular disease in the Asia-Pacific region. *J Hypertens*. 2007;1:73-9.
- 7 Martiniuk AL, Lee CM, Lam TH, Huxley R, Suh I, Jamrozik K, et al; Asia Pacific Cohort Studies Collaboration. The fraction of ischaemic heart disease and stroke attributable to smoking in the WHO Western Pacific and South-East Asian regions. *Tob Control*. 2006;15:181-8.
- 8 Woodward M, Lam TH, Barzi F, Patel A, Gu D, Rodgers A, et al; Asia Pacific Cohort Studies Collaboration. Smoking, quitting, and the risk of cardiovascular disease among women and men in the Asia-Pacific region. *Int J Epidemiol*. 2005;34:1036-45.
- 9 Boedhi-Darmojo R, Setianto B, Sutedjo, Kusmana D, Andradi, Supari F, et al. A study of baseline risk factors for coronary heart disease: results of population screening in a developing country. *Rev Epidemiol Sante Publique*. 1990;38:487-91.
- 10 Critchley JA, Capewell S. Mortality risk reduction associated with smoking cessation in patients with coronary heart disease: a systematic review. *JAMA*. 2003;290:86-97.
- 11 Yoon KH, Lee JH, Kim JW, Cho JH, Choi YH, Ko SH, et al. Epidemic obesity and type 2 diabetes in Asia. *Lancet*. 2006;368:1681-8.
- 12 Pan WH, Yeh WT, Weng LC. Epidemiology of metabolic syndrome in Asia. *Asia Pac J Clin Nutr*. 2008;17(Suppl 1):37-42.
- 13 Adam FM, Adam JM, Pandelegi N, Mappangara I. Asymptomatic diabetes: the difference between population-based and office-based screening. *Acta Med Indones*. 2006;38:67-71.
- 14 Eppens MC, Craig ME, Jones TW, Silink M, Ong S, Ping YJ; The International Diabetes Federation Western Pacific Region Steering Committee. Type 2 diabetes in youth from the Western Pacific region: glycaemic control, diabetes care and complications. *Curr Med Res Opin*. 2006;22:1013-20.
- 15 De Luca G, Suryapranata H, Ottavanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. *Circulation*. 2004;109:1223-5.
- 16 Jacobs AK, Antman EM, Ellrodt G, Faxon DP, Gregory T, Mensah GA, et al. Recommendation to develop strategies to increase the number of ST-segment-elevation myocardial infarction patients with timely access to primary percutaneous coronary intervention. *Circulation*. 2006;113:2152-63.
- 17 Stone GW. Angioplasty strategies in ST-segment-elevation myocardial infarction. Part I: primary percutaneous coronary intervention. *Circulation*. 2008;118:538-51.
- 18 Hidayat B, Thabrany H, Dong H, Sauerborn R. The effects of mandatory health insurance on equity in access to outpatient care in Indonesia. *Health Policy and Planning*. 2004;19:322-35.
- 19 Thabrany H, Gani A, Pujiyanto, Mayanda L, Muhlil, Budi BS. Center for Health Economic Studies, University of Indonesia, Presented in Social Health Insurance Workshop, WHO SEARO, New Delhi, March 13-15, 2003.
- 20 De Boer MJ, van Hout BA, Liem AL, Suryapranata H, Hoorntje JCA, Zijlstra F. A cost-effective analysis of primary coronary angioplasty versus thrombolysis for acute myocardial infarction. *Am J Cardiol*. 1995;76:830-3.