The management of acute myocardial infarction in developing countries

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Received 13 May 2005; received in revised form 19 September 2005; accepted 5 November 2005
Available online 20 December 2005

Abstract

Developing countries contribute a major share to the global burden of cardiovascular disease. Acute myocardial infarction (AMI) in particular remains one of the leading causes of death in the developing world as well as in the developed world. While the risk factors, management and outcome of AMI have been extensively studied in the developed world, limited data is available on this subject from developing countries. The current review looks at the prevalence of the classical coronary artery disease risk factors in developing countries and their association with myocardial infarction, as well as the management and outcome of AMI patients in these countries.

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Keywords: Developing countries; Coronary artery disease risk factors; Acute myocardial infarction

1. The risk factors

The World Health Organization (WHO) has recently reported an extensive study on cardiovascular diseases. The data was collected from established datasets from the United Nations system and published in “The Atlas of Heart Disease and Stroke” [1]. The percent contribution of the classical CAD risk factors to the overall burden of disease in developing countries was as follows: smoking (12%), hypertension (9%), obesity (7%), diabetes and dyslipidemia (7%). Together, these risk factors accounted for 75% of the cardiac disease burden [1], implying that 75% of patients with cardiac disease have at least one of these risk factors. Recent studies suggest that the strength of association between CAD risk factors and AMI vary between populations. Van den Hoogen et al. examined the risk of death from CAD in relation to blood pressure in six different
populations around the world [6]. The study followed 12,031 men who were free from CAD in seven countries (USA, Finland, Netherlands, Italy, Greece, Yugoslavia, Japan) over a period of 25 years. The relative increase in mortality due to CAD in relation to blood pressure was similar, but the absolute risk at a given blood pressure varied substantially among these populations. The INTERHEART is another large international case-control study designed to assess the strength of association between various risk factors and AMI and to check if this association varies with geographic location. Participants were recruited from 256 centers in 52 countries in Asia, Europe, the Middle East and South America. 15,152 cases of first AMI patients and 14,820 age and sex matched controls were enrolled [7]. The risk factors analyzed were smoking, reported history of diabetes or hypertension, ApoB/ApoA1 ratio, psychosocial stressors, exercise and alcohol intake. The population attributable risk (PAR) for diabetes varied from 7.2% in Australia to 21% in Southeast Asia. Similarly, the PAR for hypertension varied from 9.2% in the Middle East to 38.4% in Southeast Asia. Again, this study confirmed the variability in prevalence and impact on CAD development among different populations.

1.1. Diabetes

According to the WHO, the most recent estimates reveal that the prevalence of diabetes in developing countries is 4% as compared to 6% in developed countries. The prevalence of diabetes is 7.8% in the North American region and the Middle East, 5.3% in Southeast Asia and 3.7% in South America [8]. According to the INTERHEART study, a reported history of diabetes was found in 18% of AMI cases as compared to 8% in controls and the odds ratio for developing MI in diabetics was 2.4 after adjusting for all other risk factors [7]. China alone accounts for 50% of the total number of diabetics worldwide even though the prevalence of diabetes was only 1% in early 1990s [9]. Yet, the prevalence of diabetes among Chinese patients with AMI is comparable to that in AMI patients in western countries (Europe, North and South America) as reported by the GRACE (Global Registry of Acute Coronary Events) and NRMI (National Registry of Acute Myocardial Infarction-USA) Registries (Table 1) [10–12]. AMI patients from the Middle Eastern and gulf regions have a higher prevalence of diabetes when compared to other regions as specified in Table 1. In India, the prevalence of diabetes varies from 8% in urban areas to 0.4% in rural areas [13].

1.2. Hypertension

A recent study by Kearney et al. looking at age and sex specific prevalence of hypertension in representative population samples worldwide estimated the total number of people with hypertension in year 2000 to be 972 million (26.4% of the total adult population), of which two thirds are in economically developing countries [14]. The INCLEN study (Multicenter Collaborative Study in the International Clinical Epidemiology Network) looked at 12 samples (composed of 200 men each) from 7 developing countries (China, Thailand, the Philippines, Indonesia, Chile, Colombia and Brazil) to determine the prevalence of cardiovascular risk factors. In 6 out of the 12 samples, more than 20% of those surveyed had SBP >160 mm Hg and/or DBP >95 mm Hg [2]. The “Seven Countries Study Research Group” followed up 12,000 men with hypertension over a period of 25 years. Mortality from CAD was 70 per 10,000 person years in the USA and North Europe compared to only 20 per 10,000 person years in Japan and South Europe [6], thus showing that hypertension contributes differently to mortality from CAD in different countries. Similarly, the INTERHEART study which included more than 30,000 patients in 52 countries concluded that classical risk factors contribute differently to AMI risk in different populations [7]. The prevalence of hypertension in AMI patients in the GRACE and NRMI registries was similar to what is reported from Brazil and Lebanon (Table 1). In Ethiopia and China, the incidence of hypertension among patients with AMI is 47% (Table 1).

1.3. Hyperlipidemia

Many studies attribute the growing burden of CAD to the urbanization of diet in the developing countries [15–17]. The INCLEN study revealed that many developing countries had a higher than normal cholesterol level, reaching > 6.5 mmol/L in 20% of the 12 samples selected. A recent study from Beijing attributed a significant rise in

| Risk factor profile of patients presenting with acute myocardial infarction |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Diabetes                   | 34%                          | 21%                         | 22%                         | NR                          | 12%                         | 23%                         | 29%                         |
| Dyslipidemia               | 46%                          | NR                          | NR                          | 69%                         | 17%                         | 38%                         | 31%                         |
| Hypertension               | 52%                          | 47%                         | 54%                         | 47%                         | 24%                         | 54%                         | 56%                         |
| Smoking                    | 56%                          | 63%                         | 42%                         | NR                          | NR                          | 59%                         | 26%                         |
| Mean age                   | 65 years                     | 63 years                    | 56 years                    | 55 years                    | NR                          | 65 years                    | 68 years                    |

NR = not reported.
CAD mortality to each 1 mmol/L increase in total cholesterol [17]. Yet recent results from Sino Monica (a 7-year study monitoring trends and determinants of cardiovascular disease in geographically defined populations in different parts of China) indicate that cholesterol level in China is low relative to western countries [18]. The mean cholesterol level in China was 4.14–5.27 mmol/L. This would stress the fact that incremental changes in cholesterol level probably have more effect on mortality than absolute cholesterol levels. Literature review reveals that the prevalence of hypercholesterolemia is quite variable among patients with AMI in different regions (Table 1). It is exceptionally very low in India at 17%, whereas it is highest in Ethiopia (69%). According to a previous study about AMI patients in different parts of China, hypercholesterolemia was not a significant risk factor for AMI [19]. Yet recent results from INTERHEART reveal that hypercholesterolemia (high ApoB/ApoA levels) is a significant risk factor for AMI in Southeast Asia.

1.4. Age

Recent trends in the developed world reveal a shift in the age distribution of AMI patients with a 29% increase in AMIs occurring in patients more than 80 years old [20]. On the other hand, the mean age of AMI patients in developing countries ranges from 55 to 65 years, which is lower than that in the developed world (65–68 years) as reported by the GRACE and NRMI registries (Table 1). According to the INTERHEART study [7], the median age of women presenting with the first AMI is 9 years more than that of men. The youngest population of AMI patients was found in South Asia (53 years) and the Middle East (51 years), whereas the eldest was in China and Hong Kong (63 years).

1.5. Smoking

At present there are about 5 million deaths a year worldwide due to tobacco-related diseases, half of which are in developing countries. By 2030, if present trends continue unchecked, the figure will increase to 10 million deaths per year, with 70% of these deaths occurring in developing countries [21]. Although the incidence of smoking has been decreasing in men in the developed world, this has not been the case in developing countries where that incidence is actually on the rise [22]. The incidence of smoking in women, however, has been increasing worldwide [22]. According to the INTER-HEART study, smoking was the most important risk factor for AMI globally [7]. The INCLEN trial revealed the highest smoking rates among Chinese and south Asians, whereas smoking was less prevalent among the South American populations. The National survey in China indicates that 63% of men smoke compared to 3.8% of women [3]. Table 1 shows that more than 40% of patients with AMI have been smokers for some time in their lives. Recent efforts to reduce the devastating health and economic impacts of smoking lead to the WHO-FCTC (Framework Convention on Tobacco Control). The treaty was negotiated by the 192 member states of the World Health Organization (WHO). The treaty includes financial and political support for developing countries to implement anti-smoking policies [21].

1.6. Obesity

In the recent years, obesity has emerged as a major risk factor for coronary artery disease. In the developing world, it is estimated that one third of the population is obese [23]. The risk of developing coronary artery disease in obese patients is estimated to be about three times more than in those with normal body weight [23]. In the past, it was felt that obesity is a disease of the developed world. However, it has become evident recently that obesity is also a major health care burden in the developing world as well. In a recent study from 36 developing countries, the prevalence of overweight was higher than underweight among young women (20–49 years) [24]. Furthermore, although in the past obesity in the developing world was thought to be concentrated in the group with high socioeconomic class, recent data shows that obesity is now spreading in all socioeconomic classes in these countries [25]. Clearly, obesity is becoming a major health care burden in all socioeconomic classes in developing countries. However, the association of obesity with cardiovascular risk in these countries has not been yet well studied, unlike the case in the developed world.

2. Medical therapy in AMI

The pharmacological therapy of AMI has progressed significantly in the past decade. Most developed countries have established large and extensive national registries that document the use of the various medications as well as interventional procedures in AMI patients. Unfortunately, such registries are practically non-existent in the developing world and most of the data available regarding AMI management in these countries is derived from small studies from single centers. All the studies mentioned in this section were observational prospective or retrospective studies that simply reported the use of certain drugs from review of the medical records of patients. One study in India evaluated the treatment practices for AMI, and its appropriateness based on ACC/AHA (American College of Cardiology/American Heart Association) guidelines [26]. Thrombolysis, β-blockers and angiotensin converting enzyme (ACE) inhibitors were used in 63%, 47% and 38%, respectively, of 1072 patients. However, when evaluated according to ACC/AHA guidelines, appropriate use was noted in 83%, 78% and 99%, respectively. The decision on use of ACE inhibitors was appropriate in most patients. Aspirin was used in 96% of patients.
A study in Brazil was done to determine the most commonly used medications in AMI [27]. The results were: aspirin (71%), nitrates (61%), diuretics (51%), ACE inhibitors (46%), thrombolytic therapy (39%) and β-blockers (35%). The study concluded that some medications that are undoubtedly beneficial have been under-used after acute myocardial infarction. In another cross-sectional study involving the hospitals of the Brazilian National Health System (SUS) in the municipal district of Rio de Janeiro, the investigators analyzed the utilization patterns of pharmacological interventions in AMI and their corresponding effects on in-hospital mortality [28]. There was a significant variation in the use of thrombolytic therapy, β-blockers, ACE inhibitors, calcium antagonists and heparin among hospitals of different juridical nature. There was underutilization of some interventions with well-established efficacy (thrombolytic therapy, aspirin, β-blockers and intravenous nitrates).

One study from Lebanon [29] showed that 51% of AMI patients received thrombolytic therapy. At discharge, 80% of the patients were given aspirin, 35% were given β-blockers, 34% were given ACE inhibitors and 30% were given statins. The above data reveal the underuse of medical therapy with β-blockers and statins. The national registry in Mexico showed that Aspirin and heparin were prescribed in 70% of MI patients at entry to the ward and the same percentage of patients received aspirin after discharge [30]. Statins have become standard therapy in patients with acute myocardial infarction in view of recent clinical trials showing their benefit in patients with CAD regardless of their cholesterol levels [31]. However, most of the studies from developing countries did not report on the use of statins. In one study from Lebanon [29], statins were utilized in 30% of AMI patients, clearly showing an underutilization of these important medications.

The primary modality for opening up occluded arteries in AMI remains thrombolysis in developing as well as developed countries. Many developing countries are not able to provide enough cardiac catheterization laboratories to support programs for primary angioplasty as a primary modality of treatment for AMI. This is why the use of thrombolytic therapy remains mainstay of treatment for ST elevation MI in these countries and it is higher than what is reported in developed countries (Table 2). However, there is still underutilization of thrombolysis even in eligible patients. The national registry in Mexico showed that only 50% of the eligible patients with ST-segment-elevation myocardial infarction received thrombolytic therapy [30]. Similarly, a study in Pakistan in a tertiary care center revealed that 30% of patients eligible for therapy with streptokinase did not receive it [32]. In addition to the underutilization of thrombolysis, several reports showed a significant delay in receiving thrombolytic therapy, mainly due to pre-hospital delay. One study in India [33] showed that the corrected mean pain-to-door time was 8.5 h. The mean door-to-drug times were 1.2 h. Out of 104 patients, 38 did not receive thrombolytic therapy. In those who did not receive thrombolytic therapy, prior therapy at local health centers, lack of knowledge of symptoms and transportation problems were the main reasons for hospital delay. In women, there was a trend for delay in time to thrombolysis and a general tendency to delay seeking help (median time to hospital arrival was 5.3 h in women compared to 5 h in men). There are similar reports about delay in thrombolysis secondary to late hospital presentation in Malaysia and Saudi Arabia [34,35]. The hospital type also has an impact on the treatment practice being followed for acute myocardial infarction. One study in India showed that government hospitals were less likely to thrombolysate a patient as compared to private, industrial and voluntary hospitals. Hospitals affiliated with a medical school followed guidelines for use of thrombolysis and β-blockers more closely than non-teaching hospitals [26].

Overall, there seems to be clear underutilization of several medications with proved efficacy such as aspirin, heparins, β-blockers, ACE inhibitors and statins in developing countries. The reasons for this are not clear. One possible cause is certainly the cost of some of the new medications, which represent a major health care burden in these countries.

Table 2

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<tbody>
<tr>
<td>Aspirin</td>
<td>96%</td>
<td>87%</td>
<td>71–87%</td>
<td>80%</td>
<td>NR</td>
<td>70%</td>
<td>NR</td>
<td>NR</td>
<td>92%</td>
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<tr>
<td>Heparin</td>
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<td>22%</td>
<td>64–82%</td>
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<td>NR</td>
<td>70%</td>
<td>NR</td>
<td>NR</td>
<td>62%</td>
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<td>Ib/IIa</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>17%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<td>21%</td>
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<tr>
<td>B-blocker</td>
<td>47%</td>
<td>58%</td>
<td>35–53%</td>
<td>35%</td>
<td>NR</td>
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<td>NR</td>
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<td>78%</td>
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<td>Ca-blocker</td>
<td>NR</td>
<td>14%</td>
<td>31%</td>
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<tr>
<td>Nitrates</td>
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<td>92%</td>
<td>61–82%</td>
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<td>NR</td>
<td>NR</td>
<td>80%</td>
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<tr>
<td>ACE inhibitor</td>
<td>38%</td>
<td>9%</td>
<td>46–63%</td>
<td>34%</td>
<td>51%</td>
<td>NR</td>
<td>NR</td>
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<td>55%</td>
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<tr>
<td>Statin</td>
<td>NR</td>
<td>NR</td>
<td>30%</td>
<td>50%</td>
<td>NR</td>
<td>17%</td>
<td>NR</td>
<td>NR</td>
<td>47%</td>
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<tr>
<td>Thrombolitics</td>
<td>63%</td>
<td>18%</td>
<td>20–39%</td>
<td>51%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>29%</td>
<td>47%</td>
</tr>
</tbody>
</table>

NR = not reported.
3. Interventions and outcomes

Unlike developed countries, data on the use of diagnostic and therapeutic procedures in AMI patients in developing countries is very scarce. In one study from a tertiary referral university hospital in Lebanon, 72% of AMI patients underwent cardiac catheterization, 23% underwent percutaneous coronary interventions and 13% underwent bypass surgery [29]. Only 0.5% of patients underwent stress testing post AMI. In another study from Pakistan, 28% of patients underwent catheterization and 16% had stress testing [32].

Studies in developed countries show an obvious decline in mortality from coronary artery disease over the past two decades [36]. In some developing countries, like Saudi Arabia, mortality rates are low (4%), approaching that of developed countries [34]. This could be either due to the facilities that are readily available in these countries or due to sample selection bias. The in-hospital mortality ranged from 18% in India, 13–20% in Brazil, to 13% in Lebanon and 11% in Pakistan, compared to only 8–9% in developed countries [37–41]. The predictors of mortality from myocardial infarction are also variable. One study in India revealed that smoking and diabetes were the most important predictors of mortality with 21% mortality in diabetics as compared to 11% in non-diabetic patients [37]. Smoking was an important predictor of death in Brazil as well, in addition to hypertension, age and cardiogenic shock [27]. Another study in Brazil reported that Killip class >1 was the most important predictor of mortality followed by advanced age, history of stroke and anterior MI [38]. Similar data were reported in Lebanon where Killip class >1 and age >60 years were found to be important predictors of mortality [29].

4. Conclusion

Data on the management and outcome of AMI patients in developing countries is very limited and is mostly derived from small one-site studies rather than large registries. This obviously introduces a very important element of bias in the representation of the data, which has to be taken into consideration when the results are interpreted. Nevertheless, in general, there seems to be a high prevalence of the classical CAD risk factors in AMI patients in these countries. Moreover, data on the use of diagnostic and revascularization procedures in AMI patients in developing countries is very scarce as well. One would expect significant variations in the utilization of these procedures based on training, availability, cost and affordability. The classic risk factors seem to contribute differently to the morbidity and mortality of AMI in different populations. This is probably related to the variations in the genetic and environmental background among these populations. Thus, the interaction between the classic CAD risk factors and these different genetic and environmental profiles will lead to different outcomes. This implies that each country or region should study its own AMI risk profile and make preventive strategies accordingly, rather than relying on data derived from other countries. There is clearly an urgent need to develop large registries in developing countries to collect data on a wide sample of AMI patients in order to have a clear idea/plan on how to improve the management and outcome of acute myocardial infarction in these countries.

References
