Outcomes in patients with acute coronary syndrome in a referral hospital in sub-Saharan Africa

Mohamed Hasham Varwani, Mohamed Jeilan, Mzee Ngunga, Anders Barasa

Abstract

Background: Coronary artery disease and its acute presentation are being increasingly recognised and treated in sub-Saharan Africa. It is just over a decade since the introduction of interventional cardiology for coronary artery disease in Kenya. Local and regional data, and indeed data from sub-Saharan Africa on long-term outcomes of acute coronary syndromes (ACS) are lacking.

Methods: A retrospective review of all ACS admissions to the Aga Khan University Hospital, Nairobi (AKUHN) between January 2012 and December 2013 was carried out to obtain data on patient characteristics, treatment and in-patient outcomes. Patient interviews and a review of clinic records were conducted to determine long-term mortality rates and major adverse cardiovascular events.

Results: A total of 230 patients were included in the analysis; 101 had a diagnosis of ST-segment myocardial infarction (STEMI), 93 suffered a non-ST-segment myocardial infarction (NSTEMI), and 36 had unstable angina (UA). The mean age was 60.5 years with 81.7% being male. Delayed presentation (more than six hours after symptom onset) was common, accounting for 66.1% of patients. Coronary angiography was performed in 85.2% of the patients. In-hospital mortality rate was 7.8% [14.9% for STEMI and 2.3% for non-ST-segment ACS (NSTE-ACS, consisting of NSTEMI and UA)], and the mortality rates at 30 days and one year were 7.8 and 13.9%, respectively. Heart failure occurred in 40.4% of STEMI and 16.3% of NSTE-ACS patients. Re-admission rate due to recurrent myocardial infarction, stroke or bleeding at one year was 6.6%.

Conclusion: In our series, the in-hospital, 30-day and one-year mortality rates following ACS remain high, particularly for STEMI patients. Delayed presentation to hospital following symptom onset is a major concern.

Keywords: acute coronary syndromes, myocardial infarction, outcomes, Kenya, sub-Saharan Africa

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The burden of cardiovascular diseases (CVD) in sub-Saharan Africa (SSA) is rapidly increasing, with a rising prevalence of cardiovascular risk factors.1-3 In SSA, CVD occurs in younger patients who are often in the working age group, thereby having a significant economic bearing.4 Coronary artery disease (CAD), once thought to be rare among native Africans, is increasingly being diagnosed.5,6 In a recent prospective survey carried out at an urban hospital in Kenya, acute coronary syndromes (ACS) contributed to 5.1% of all admissions to the critical care units.7 An autopsy study by Ogeng’go et al. reported that cardiovascular deaths comprised 13.2% of all autopsies performed during the study period.8 Among these, the leading aetiology was myocardial infarction (18.7%). The findings of these more recent studies contrast with reports from the 1960s that suggested a very low prevalence of CAD.9

It is nearly a decade since the introduction of coronary interventions and coronary surgery in Kenya. The supporting infrastructure for emergency response and intervention, however, lags behind. Most cardiovascular specialists and catheterisation laboratories (cathlabs) in the country are disproportionately located in Nairobi, the capital city.

Following an ACS, a patient remains at elevated risk of death and major adverse events such as heart failure, recurrent myocardial infarction, stroke and bleeding, compared to the general population.10 Over the last three decades, both short-term (in-hospital and 30-day) and long-term survival following myocardial infarction has been improving worldwide.11 This is thought to be due to improved response infrastructure, availability of better drugs and interventions for the acute phase, and use of secondary preventative therapies such as statins and beta-blockers.

Little is known about the outcomes of patients following an ACS in SSA.1 Apart from a report based on South African data from the ACCESS registry, no published studies were found that looked at out-of-hospital outcomes following ACS in SSA.12 A few local reports have described the management and in-hospital outcomes in patients with ACS.13,14 Long-term outcomes in the country and region however remain unknown.
The Aga Khan University Hospital, Nairobi, is a private teaching hospital, serving as a referral centre for patients within Kenya and the broader region of East and Central Africa. A heterogenous cohort of patients is therefore served at the facility. The cathlab operates during the daytime, but is available for emergencies after that, with an on-call interventional cardiologist and cathlab team.

**Methods**

The primary study objective was to determine the in-hospital and long-term (30-day and one-year) mortality rates of ACS patients treated at the Aga Khan University Hospital, Nairobi (AKUHN). Secondary objectives were to determine the rate of in-hospital non-fatal events, specifically heart failure, recurrent myocardial infarction (MI), need for repeat revascularisation, stroke and major bleeding, and to determine the rate of rehospitalisation in the first year owing to major adverse events (recurrent MI, stroke and major bleeding).

This was a cross-sectional, retrospective review of chart and electronic health records for all patients admitted with ACS between 1 January 2012 and 31 December 2013. To confirm our findings, and where chart data were ambiguous, telephone interviews were conducted with the patients and documented relatives to determine the long-term outcomes following discharge.

Ethical approval was obtained from the Ethical and Scientific Review Committee of the AKUHN. Verbal consent was obtained from the participants prior to initiating the telephone interview.

The study included patients who received a discharge diagnosis of ACS and its subcategories: ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina (UA) (ICD 10 codes I20.0, I21, I22, respectively). Patients with suspected type 2 MI were excluded.

MI was defined by the third universal definition of MI; major bleeding was defined as per the TIMI bleeding criteria, other outcome definitions were based on accepted definitions used in cardiovascular trials.

### Statistical analysis

IBM Statistical Package for Social Sciences (SPSS) version 21 was used to analyse the data. All patients were grouped into either STEMI or non-ST-elevation ACS (NSTEMI, consisting of NSTEMI or UA) for comparison of demographic and clinical characteristics, and outcome variables of interest. Continuous variables are expressed as mean ± standard deviation and comparisons between means were performed using independent samples Student’s t-test. Categorical variables are expressed as percentages, and comparisons between subgroups were performed using Fisher’s exact test.

Survival analysis was performed using Kaplan–Meier estimates. The duration from event to death was calculated for patients who died. Patients were censored at the date of last contact based on the medical records or on the date of the telephone interview, whichever was latest.

### Results

During the 24-month period, 230 patients were admitted with ACS. Of these, 101 had a STEMI, 93 suffered an NSTEMI, and 36 had UA. Demographic and clinical characteristics of the patients are summarised in Table 1.

Fewer than 10% of patients presented within one hour of symptom onset, while more than 35% took longer than 24 hours to arrive at the hospital, some taking as long as two weeks (Fig. 1). Patients with STEMI tended to present earlier, compared to those with NSTEMI, with 46.6 and 23.3% presenting within six hours of symptom onset, respectively.

Of the 101 patients admitted with STEMI, 49 received thrombolytic therapy while 19 patients underwent primary percutaneous intervention (PCI). Thirty-three patients presented

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>STEMI</th>
<th>NSTEMI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEMI</td>
<td>101</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>STEMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSTEMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>STEMI</th>
<th>NSTEMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>58.7 ± 13.8</td>
<td>61.9 ± 12.0</td>
</tr>
<tr>
<td>Male gender, %</td>
<td>81.2</td>
<td>82.2</td>
</tr>
<tr>
<td>Diabetics, %</td>
<td>43.6</td>
<td>31.0</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>52.5</td>
<td>64.3</td>
</tr>
<tr>
<td>Smoker, %</td>
<td>22.8</td>
<td>23.3</td>
</tr>
<tr>
<td>Creatinine, μmol/l</td>
<td>108.6 ± 60.7</td>
<td>103.8 ± 45.3</td>
</tr>
<tr>
<td>Creatinine clearance (Cockcroft–Gault), ml/min/1.73 m²</td>
<td>84.2 ± 38.4</td>
<td>82.7 ± 37.1</td>
</tr>
<tr>
<td>Total cholesterol, mmol/l</td>
<td>4.6 ± 1.4</td>
<td>4.5 ± 1.4</td>
</tr>
<tr>
<td>HDL, mmol/l</td>
<td>1.1 ± 0.3</td>
<td>1.1 ± 0.3</td>
</tr>
<tr>
<td>LDL, mmol/l</td>
<td>2.9 ± 1.3</td>
<td>2.8 ± 1.2</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.6 ± 4.1</td>
<td>28.1 ± 5.1</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>127 ± 28</td>
<td>140 ± 24</td>
</tr>
<tr>
<td>Pulse rate per minute</td>
<td>88 ± 19</td>
<td>79 ± 17</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black African, %</td>
<td>33.7</td>
<td>34.9</td>
</tr>
<tr>
<td>Caucasian, %</td>
<td>4.0</td>
<td>9.3</td>
</tr>
<tr>
<td>Asian Indian, %</td>
<td>62.4</td>
<td>55.8</td>
</tr>
</tbody>
</table>

**Table 1. Demographic and clinical characteristics of patients**

**Statistical analysis**

IBM Statistical Package for Social Sciences (SPSS) version 21 was used to analyse the data. All patients were grouped into either STEMI or non-ST-elevation ACS (NSTEMI, consisting of NSTEMI or UA) for comparison of demographic and clinical characteristics, and outcome variables of interest. Continuous variables are expressed as mean ± standard deviation and comparisons between means were performed using independent samples Student’s t-test. Categorical variables are expressed as percentages, and comparisons between subgroups were performed using Fisher’s exact test.

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**Results**

During the 24-month period, 230 patients were admitted with ACS. Of these, 101 had a STEMI, 93 suffered an NSTEMI, and 36 had UA. Demographic and clinical characteristics of the patients are summarised in Table 1.

Fewer than 10% of patients presented within one hour of symptom onset, while more than 35% took longer than 24 hours to arrive at the hospital, some taking as long as two weeks (Fig. 1). Patients with STEMI tended to present earlier, compared to those with NSTEMI, with 46.6 and 23.3% presenting within six hours of symptom onset, respectively.

Of the 101 patients admitted with STEMI, 49 received thrombolytic therapy while 19 patients underwent primary percutaneous intervention (PCI). Thirty-three patients presented
outside the acute phase and did not receive acute reperfusion therapies. The mean time to thrombolysis and PCI was 49 (± 42) and 137 (± 63) minutes, respectively.

Target door-to-needle time for thrombolysis of 30 minutes was met in 26 of the 49 patients thrombolysed (53.1%), and door-to-balloon time of 90 minutes in five of the 19 patients taken for primary PCI (26.3%).

One hundred and ninety-six of 230 (85.2%) patients underwent coronary angiography. The left anterior descending artery was the most common culprit vessel, accounting for 51.6% of STEMI and 37.8% of NSTE-ACS. Non-occlusive coronary artery disease was found to be the underlying cause of ACS in two patients with STEMI and three with NSTE-ACS. Of the 196 patients, 64 (32.8%) were found to have multi-vessel disease.

Of the 230 patients, 219 had documented left ventricular function assessment done by two-dimensional echocardiography. Left ventricular ejection fraction (LVEF) of patients with STEMI was significantly lower than that of NSTE-ACS patients (42.2 vs 50.3%, p < 0.001). One patient with STEMI and three with NSTE-ACS were readmitted with a stroke, and three patients were admitted due to major bleeding.

**Discussion**

With increasing awareness of the problem and access to expertise and facilities, management of ACS in East and Central Africa has seen some evolution in the past decade. In 2006, there were only two functioning cathlabs in the region, both located in Kenya. By 2012 this number grew to five, and in 2017 there were 12 cathlabs located within three countries in the region. A few reports have described management practices and in-hospital outcomes. However this is the first study in the region that reports on both in- and out-of-hospital outcomes in patients who have suffered ACS.

The mean age of patients was 60.5 (± 12.8) years. This is comparable to the mean age in the South African cohort in the ACCESS-SA study, but about four years younger than that reported in a European registry, the EHS-ACS-II. This supports the notion that ACS is occurring at a younger age in patients from SSA compared to western countries. Notably in both the ACCESS-SA and EHS-ACS-II studies, STEMI patients were significantly younger than patients with NSTE-ACS (54.5 vs 60.5 years, and 62.5 vs 66.1 years, respectively). This difference was however much less pronounced in our study (58.7 and 61.9 years, respectively, p = 0.063).

As in other studies, an overwhelming male predominance was noted in both subgroups. There were no significant differences between the two groups with regard to other patient characteristics, and these were comparable to those noted in other studies.

In this study, 230 patients had a confirmed diagnosis of ACS in the two-year period from January 2012 to December 2013. This is more than twice the number of ACS admissions reported at the same facility between April 2008 and May 2010, reflecting the growing number of ACS patients seen and managed at the centre.

STEMI comprised 44% of the patients presenting with ACS in this study. This is comparable to data from both the EHS-ACS-II and ACCESS-SA registries, in which STEMI accounted for 47 and 41% of the patients’ diagnosis, respectively.

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**Table 2. In-hospital events**

<table>
<thead>
<tr>
<th>Events</th>
<th>STEMI (n = 101)</th>
<th>NSTE-ACS (n = 129)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, n (%)</td>
<td>15 (14.9)</td>
<td>3 (2.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Heart failure, n (%)</td>
<td>40 (40.4)</td>
<td>21 (16.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>1 (1)</td>
<td>3 (2.3)</td>
<td>0.64</td>
</tr>
<tr>
<td>Major bleed, n (%)</td>
<td>2 (2)</td>
<td>2 (1.6)</td>
<td>1</td>
</tr>
<tr>
<td>Repeat revascularisation, n (%)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 2. Kaplan–Meier curves for survival.**

- **Diagnosis**
  - STEMI
  - NSTE-ACS
  - STEMI-censored
  - NSTE-ACS-censored

**Log Rank**

<table>
<thead>
<tr>
<th>Test</th>
<th>df</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breitlow</td>
<td>6.915</td>
<td>1</td>
</tr>
<tr>
<td>Tarone-Ware</td>
<td>5.726</td>
<td>1</td>
</tr>
</tbody>
</table>

**Outcomes**

Heart failure was the most common in-hospital complication and was more likely to occur in STEMI patients (40.4 vs 16.3%, p < 0.001). One patient with STEMI and three with NSTE-ACS suffered a stroke, while two patients in each category developed a major bleed.

Survival status and out-of-hospital outcome data were obtained in 184 of 212 patients (86.8%) discharged alive from hospital. At the end of 30 days, 7.8% of the patients had died, and at the end of one year after the event, 13.9% had died. The mortality rate at both 30 days (13.7 vs 3.1%) and one year (20.8 vs 8.5%) was higher in patients with STEMI compared to those with NSTE-ACS.

Kaplan–Meier survival curves for STEMI and NSTE-ACS are displayed in Fig. 2. There was an early and significant separation of the curves, and while this reduced over the course of time, the difference remained significant at the end of 50 months of follow up (Fig. 2).

A total of 14 of the 212 patients discharged alive (6.6%) were readmitted during the first year following the event. Of these, 10 patients suffered a recurrent myocardial infarction; one patient was readmitted with a stroke, and three patients were admitted due to major bleeding.
The most prominent major modifiable risk factor in our population was hypertension, present in nearly 60% of the patients. This is consistent with data from other regional and international series. Diabetes appeared more prevalent (36.5%) in our series than in other series (23.9% in ACCESS-SA and 14.1% in EHS-ACS-II). By contrast, smokers accounted for less than a quarter of the ACS cases in our series, compared to nearly double that in both of the above series.

In our study, we considered established atherosclerotic coronary disease as either prior MI or a revascularisation procedure. It was notable that this was significantly higher in patients with NSTE-ACS compared to the STEMI group (28.7 vs 5.9%, \( p < 0.001 \)). ACS registries and other prospective surveys have looked at MI, PCI and coronary artery bypass grafting (CABG) separately. In the EHS-ACS-II series, a prior MI was reported in 15.7% of patients with STEMI and nearly double that with NSTE-ACS. Similarly, a revascularisation procedure had been performed in only 8.9% of STEMI and 21.5% of NSTE-ACS patients. This suggests that patients who have pre-existing coronary artery disease are more likely to present with NSTE-ACS than STEMI. These data need to be understood in the context of the relatively recent availability of facilities for diagnosis and coronary intervention in our region.

In this study, fewer than 10% of the patients presented within one hour of symptom onset and more than 35% presented more than 24 hours later. The median time to presentation was more than 12 hours. By contrast, the median time to presentation in the the EHS-ACS-II series was less than three hours, while in the ACCESS-SA study, the median time to presentation was 3.6 and 7.4 hours for STEMI and NSTE-ACS, respectively.

Prompt treatment from symptom onset, especially in STEMI, is a key determinant of patient outcomes in ACS.\(^4\) There is a significant delay in presentation to hospital in our set-up and this is an important factor to address. STEMI systems of care are rudimentary or non-existent in SSA and outcomes can be expected to be poor in this group of patients where delays to reperfusion occur.

Reasons contributing to late presentation are probably multifactorial and must be studied systematically in SSA, given the unique challenges faced by patients. In many cases, a lack of appreciation for the significance of the symptoms by the patient and/or their initial point of medical contact, or a lack of ACS diagnostic facilities (ECG or cardiac enzymes) will result in a significant delay between onset of symptoms and arrival at a facility capable of managing STEMI.

Public education and awareness programmes have been effective in tackling this in countries with developed ACS infrastructure. Heightened sensitivity within the healthcare fraternity targeting such facilities may facilitate early diagnosis. Moreover, a structured referral system that integrates treatment strategies, such as pre-referral thrombolysis and emergency medical technician (EMT) services, would help to reduce delays in treatment and improve outcomes.

In the study, 48.5% of patients with STEMI received thrombolysis, 15.8% were subjected to primary PCI, and no acute reperfusion was performed in nearly 35% of patients, primarily due to delayed presentation. This contrasted with the strategies employed in the EHS-ACS-II series in which, of the 63.9% of patients who received primary revascularisation treatment, a greater proportion (51.8%) of patients was treated with primary PCI. The low rate of primary PCI compared to thrombolysis might reflect the absence of a 24-hour on-site team, and a perceived delay in arrival of the on-call team. Given the low volume of primary PCI in most cathlabs in the region, it is not yet cost effective to have an on-site team.

However, when considering the temporal trends within our unit, the rate of primary PCI has increased nearly two-fold from that reported by Shavadia et al. in the 2008–2010 series. This reflects the increased availability of interventional expertise and may also reflect established processes to facilitate delivery of these services within the unit.

STEMI patients in our series had a higher mortality rate compared to other series.\(^{11,19}\) As discussed, a large proportion of patients in our series had a significant delay from onset of symptoms to hospital presentation, with more than half presenting more than 12 hours after symptom onset. It is well known that outcomes in STEMI are strongly related to the promptness of acute reperfusion therapy, therefore delayed presentation of patients may account for the increased in-hospital and long-term mortality rates compared to other series.

The STEMI group had a significantly lower LVEF and were also more likely to develop heart failure while in hospital compared to NSTE-ACS patients. This implies that significant myocardial damage had occurred in a significant proportion of these patients.

In a series that reported on long-term outcomes, early mortality rate was often higher in STEMI patients, but by the end of one year, this was usually similar to or lower than in NSTE-ACS patients.\(^5\) In our series, we noted a higher STEMI mortality rate, even at the end of one year. Also, the Kaplan–Meier survival estimates suggest a significantly higher STEMI mortality rate even beyond one year. Again, this may be associated with significant myocardial damage that occurs in patients with STEMI, predisposing them to long-term mortality.

Heart failure or cardiogenic shock was the most common in-hospital complication occurring in 26.5% of patients, with STEMI patients twice as likely to develop this. In the EHS-ACS-II series, this occurred in a significantly lower proportion of patients (12.4%). Delays in presentation and revascularisation could explain this.

Patient-reported readmissions due to the pre-specified major adverse events at one year occurred in 14 of the 212 (6.6%) patients discharged alive. Recurrent MI occurred in 10 patients, stroke in one and bleeding requiring hospitalisation in three patients. In the ACCESS registry, 15.6% of patients were readmitted due to a cardiac-related event in the first year. Of these, nearly two-thirds were admitted due to recurrent ACS, 15% due to heart failure, 1.8% due to bleeding and 6.6% due to stroke or transient ischaemic attack.

We acknowledge that our series was subject to reporting bias and the common limitations of retrospective analysis. However, our response rate of 86.8% would indicate that a representative group completed follow up. The study was conducted in an urban, private, tertiary-level referral facility and therefore the patient population seen here is vastly different from the general population in Kenya. The results of this study should be interpreted with this in mind. However, the facility is one of the few hospitals in the region that has a well-developed cardiology programme and this study provides previously unavailable data on the short- and long-term outcomes of ACS in the region.
Conclusions
This single-centre report from an urban referral hospital in SSA suggests that in-hospital and long-term mortality rates following ACS, particularly STEMI, remain high. Delayed presentation following symptom onset appears to be an important contributing factor. This needs to be studied systemically and tackled, keeping in mind local challenges. STEMI preparedness strategies and innovative homegrown solutions should become an area of focus for healthcare providers coming to terms with the expected epidemic of coronary artery disease in SSA.

References