Clinical outcome of older patients with acute coronary syndrome over the last three decades

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Abstract

Objective: to evaluate the clinical outcome of patients with acute coronary syndrome (ACS) in the Coronary Care Unit (CCU) over three decades in Dunedin, New Zealand.

Design: registry study.

Setting and patients: all consecutive patients (n = 3,013) with ACS admitted to the CCU from 1979 to 1981 (n = 966) and from 1989 to 1991 (n = 1470) were included prospectively. Data on ACS patients managed in the CCU in 2001–2002 (n = 577) were obtained via medical chart review.

Results: there was a rising proportion of older (≥75 years of age) patients with ACS (3.8% in 1979–1981, 15.2% in 1989–1991 and 25.6% in 2001–2002, P<0.0005). However, we observed a progressive reduction of in-hospital mortality for ACS (10.7, 7.3 and 5.0%, P<0.005) and for ST-elevation myocardial infarction (STEMI) (18.4, 16.1 and 6.6%, P<0.005). The progressive fall in mortality rate was also observed amongst older patients, both for ACS (27, 19.2 and 11.5%, P = 0.011) and for STEMI (34.8, 30.9 and 15.4%, P<0.005). Of concern, only 10% of patients presented within 1 h of symptom onset and 50% within 5 h, and this has not changed over three decades. The variables associated with <5 h from symptom onset to presentation were men [odds ratio (OR) 1.25, 95% confidence interval (CI) 1.10–1.42, P = 0.001], a history of ischaemic heart disease (OR 1.25, 95% CI 1.09–1.43, P = 0.002) and STEMI (OR 1.41, 95% CI 1.18–1.67, P<0.0001). Advanced age was not a predictor for late presentation.

Conclusions: over the past three decades, more old patients were treated in the CCU. However, there was a decline in hospital mortality, particularly for STEMI. Further efforts are required to decrease the time to presentation.

Keywords: acute coronary syndrome, changing demography, cardiovascular outcome, elderly

Introduction

Over the last three decades, the management of acute coronary syndrome (ACS) has improved [1–3]. We have witnessed lengthened human longevity [4–6] and an increased public awareness of heart attacks [5,7]. As a result, the demography of patients presenting with ACS has changed and so has the hospital mortality [8]. In Dunedin hospital, the primary teaching hospital for the University of Otago and the tertiary referral centre for the Otago and Southland regions in New Zealand, a prospective database was set up in the 1970s, collecting data until 1993 on all patients managed in the coronary care unit (CCU) [9,10].

For the current study, further data collection was done via medical chart review on patients admitted to the CCU in the years 2001–2002. The aim of this study was to evaluate how demography, treatment and outcome have changed over these years.

Methods

Study population

We collected data on all consecutive patients with ACS managed in the CCU from the prospective registry database for the years 1979–1981 (n = 966) and 1989–1991 (n = 1,470). Data on
ACS patients managed in the CCU in 2001–2002 were obtained via medical chart review (n = 577). All patients admitted into CCU in 2001–2002 were systematically recorded in a logbook, and reviewed by a single physician to obtain all relevant information from clinical records. The study was in line with our hospital policy on clinical research and data collection.

Patients with ACS were classified into three groups: ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) and unstable angina. For the first two periods, 1979–1981 and 1989–1991, STEMI was defined by having ≥1 mm of ST-elevation in two contiguous leads (or ≥2 mm if V1 to V2 leads were involved) or new left bundle branch block, together with ischaemic chest pain for >30 min and/or elevation of creatinine kinase (CK) to more than twice the upper limit. In the period 2001–2002, troponin I (Abbott AxSYM assay) of >2.0 μg/l was the marker of myonecrosis instead of CK.

The definition of NSTEMI for the periods 1979–1981 and 1989–1991 included all of the following: (i) no ST-elevation on electrocardiography (ECG) nor new left bundle branch block; (ii) CK more than twice the upper limit of normal; and (iii) chest pain for >30 min. In 2001–2002, troponin I (Abbott AxSYM assay) of >2.0 μg/l was used as a marker of myonecrosis instead of CK. The definition of unstable angina in all three periods was chest pain for >30 min without any ECG or biochemical evidence of acute myocardial infarction.

Major end-points
We analysed in-hospital mortality as the primary end-point. Left ventricular failure (LVF) during admission was considered to be present if any of the following criteria were satisfied: (i) a clinical diagnosis documented by the attending cardiologist; (ii) radiographic evidence of pulmonary or interstitial oedema; or (iii) the commencement of anti-failure therapies with the use of loop diuretics.

Other parameters
The length of time from symptom onset to presentation was recorded and divided into time intervals of <1 h, 1–4 h, 5–8 h, 9–12 h, 13–24 h, 25–48 h, 49–72 h and >72 h, based on the original codes used when the CCU registry started in 1979.

The diagnosis of diabetes for all three periods was based on patient history. Dyslipidaemia was based on patient’s history in the periods 1979–1981 and 1989–1991. In 2001–2002 when lipid data were always available, dyslipidaemia was defined as a total fasting cholesterol of ≥5.5 mmol/l. Blood pressure (BP) was considered elevated if systolic BP was ≥140 mmHg and diastolic BP was ≥90 mmHg on at least two consecutive measurements after arrival.

Statistical analysis
Statistical analysis was completed using the Statistical Program for the Social Sciences (SPSS) for McIntosh version 10.0. The χ² test for trend was used to test whether data in each of the three periods were increasing or decreasing in a linear manner. All tests were double-sided and considered statistically significant at <0.05. Multivariable analysis was performed using stepwise logistic regression.

Results
For the three periods, a total of 4,908 patients were admitted into the CCU, with ACS diagnosed in 3,013 patients, including 966 in the years 1979–1981, 1,470 in the years 1989–1991 and 577 in the years 2001–2002. Of these 3,013 patients, 1,955 were men and 1,058 were women; 2,604 were aged <75 years and 409 were aged ≥75 years.

Women and older patients
In Table 1, it can be seen that the percentage of women presenting with ACS has increased from 30.4% in 1979–1981 to 37.4% in 1989–1991, and 37.2% in 2001–2002 (P = 0.002). The proportion of older patients ≥75 years with ACS admitted into the CCU has increased from 3.8% in 1979–1981, 15.2% in 1989–1991 to 25.6% in 2001–2002 (P < 0.0005). Table 1 breaks down the age subgroups of patients admitted into our CCU (≥60, 61–74, 75–84 and ≥85). Women ≥75 years of age constituted only 0.9% of total admissions in 1979–1981. This figure rose to 6.8% in 1989–1991 and 13.2% in 2001–2002 (P < 0.0005). Combining patients from the three decades, 32% of CCU admissions were STEMI in patients aged <75 years, compared with 41% in patients aged ≥75 years (P < 0.0005).

Cardiac risk factors
Over the three decades, there was an increasing prevalence of having diabetes and dyslipidaemia but not high BP as risk factors (Table 1). In 1979–1981, 49.7% patients with ACS had BP ≥140/90 mmHg, dropping to 31.9% in 1989–1991 and to 26.2% in 2001–2002 (P < 0.0005).

In-hospital mortality rate
In-hospital mortality rates for ACS dropped across the three decades (10.7% in 1979–1981, 7.3% in 1989–1991 and 5.0% in 2001–2002, P < 0.005, Table 2). This trend of mortality reduction was seen both in patients aged <75 years (27.0,
Table 2. Mortality rate and complications for ACS and STEMI over three decades

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<td>60–74</td>
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<td>19.2%</td>
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<td>75–84</td>
<td>29.4%</td>
<td>19.3%</td>
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<td>STEMI mortality rate</td>
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<td>&lt;75</td>
<td>17.4%</td>
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<td>36.4%</td>
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<td>Overall</td>
<td>18.4%</td>
<td>16.1%</td>
<td>6.6%</td>
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<td>22.0%</td>
<td>24.6%</td>
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*The actual numbers of patients ≥85 were one patient, six patients and 19 patients, respectively, for ACS, and no patients, three patients and 11 patients for STEMI in the three periods, respectively.

19.2 and 11.5%, P = 0.01) and in patients aged <75 years (10.0, 5.2 and 2.8%, P<0.0005).

The STEMI mortality rate dropped from 18.4% in 1979–1981, to 16.1% in 1989–1991 and to 6.6% in 2001–2002 (P<0.005, Figure 1, Table 2). For patients aged ≥75 years with STEMI, mortality dropped from 34.8% in 1979–1981, to 30.9% in 1989–1991 and to 15.4% in 2001–2002, <0.005 (Figure 1, Table 2). For patients aged <75 years with STEMI, mortality was 17.4, 11.7 and 3.4%, respectively, for the three periods (<0.0005).

Reperfusion therapy and revascularisation for STEMI in the period 2001–2002

Older patients aged ≥75 years were as likely to receive thrombolytic therapy (73.1 versus 77.8%, P = 0.62), but less likely to receive coronary angiography (43.2 versus 75.9%, P<0.0001) or percutaneous coronary intervention (27.5 versus 56.6%, P = 0.0006) than patients <75 years of age. Inpatient coronary by-pass graft was performed in 2.0% of the former and 8.5% of the latter groups, P = 0.20. For patients <75 years of age, there was no difference in hospital mortality between those who had and those who did not have inpatient revascularisation (2.3 versus 2.5%, P = 0.82). However, for patients >75 years, in-hospital mortality was 4.5% in those with and 7.5% in those without in-hospital revascularisation (P = 0.084).

Heart failure

In hospital heart failure incidence was 34.8% in 1979–1981, 22.0% in 1989–1991 and 24.6% in 2001–2002 (<0.005), and the reduction was particularly obvious in patients with STEMI. For patients aged <75 years, heart failure incidence in STEMI was 50.5% (192 out of 380) in 1979–1981, 36.4% (115 out of 316) in 1989–1991 and 26.2% (38 out of 145) in 2001–2002 (<0.005). For patients ≥75 years with STEMI, 78.3% (18 out of 23) in 1979–1981, 62.6% (57 out of 91) in 1989–1991 and 51.2% (27 out of 52) in 2001–2002 (P = 0.034) developed heart failure.

Timing of hospital presentation

The proportion of patients presenting within 1 h of symptom onset was unchanged throughout the study period: 10.1% (98 out of 966) in 1979–1981, 10.7% (157 out of 1,470) in 1989–1991 and 9.3% (43 out of 461) in 2001–2002 (P = 0.60). The proportion of patients presenting within 5 h of symptom onset was also unchanged: 56.2% (543 out of 966) in 1979–1981, 49.8% (732 out of 1,470) in 1989–1991 and 60.7% (280 out of 461) in 2001–2002 (P = 0.66). The variables associated with a ’shorter’ time (<5 h) from symptom onset to presentation were men [odds ratio (OR) 1.25, 95% confidence interval (CI) 1.10–1.42, P = 0.001], a history of ischaemic heart disease (OR 1.25, 95% CI 1.09–1.42, P = 0.002) and STEMI (OR 1.41, 95% CI 1.18–1.67, P<0.0001). However, younger age (OR 1.00, 95% CI 0.99–1.00, P = 0.10), decade of study (OR 1.00, 95% CI 0.91–1.11, P = 0.95) and heart failure (OR 1.03, 95% CI 0.89–1.20, P = 0.69) were not predictors of earlier arrival at the hospital.

Discussion

Our study showed a significant fall in hospital mortality for ACS, particularly in patients with STEMI aged >75 years, over the last three decades, and this reduction occurred despite a large increase in the numbers of older patients being treated. Few studies have examined how mortality has declined over a
three-decade period. A meta-analysis on acute myocardial infarction by de Vree et al. [11] found that the average in-hospital mortality decreased from 29% in the 1960s, to 21% during the 1970s to 16% during the 1980s. The current study collected data from the mid-1970s through to 2002. For patients aged ≥75 years presenting with STEMI, mortality dropped from 34.8% in 1979–1981 to 15.4% in 2001–2002 (P<0.005). Large international registries over a shorter time period (on patients managed in the late 1980s and the 1990s) have reported a similar trend of mortality reduction [3,8,12].

Older patients

We found that the proportion of the older population aged ≥75 years with ACS managed in the CCU increased throughout the decades, and they commonly presented with STEMI. However, there are very few controlled trials focusing specifically on management of ACS in the elderly, and findings from observational studies are conflicting.

Theimans et al. [13] retrospectively examined the 210,996 patient admissions for acute myocardial infarction from the Cardiovascular Project (CCP) database in the period from February 1994 to July 1995 and identified a cohort of 7,864 patients treated for acute myocardial infarction who were deemed eligible for thrombolytic therapy (48% aged 65–75 and 34% aged 76–86). They found that patients aged 65–75 benefited from thrombolytic therapy, but patients aged 76–86 had higher mortality with than without thrombolytic therapy (crude 30-day mortality 18.0 versus 15.4% with an adjusted hazard ratio of 1.38, P = 0.003).

However, Angeja et al. [14], using the National Registry of Myocardial Infarction-2 database, found a reduced inhospital mortality with tissue plasminogen activator treatment in men up to age 84 as compared with no thrombolysis. With a longer follow-up period of 1 year, Stenestrand et al. [15] from Sweden reported that thrombolytic therapy had resulted in a 13% reduction in combined mortality and cerebral complications (P = 0.001) in 6,891 consecutive patients aged ≥75 who presented with their first STEMI (3,897 treated with and 2,994 treated without thrombolytic therapy).

In the current study, there was definitely a better survival in the latest time period (2001–2002) amongst patients ≥75 years old, as shown in Figure 1. Although younger patients showed a greater relative reduction in mortality, absolute mortality reduction was greater in patients ≥75 (Table 2). In 2001–2002, older patients with STEMI were just as likely to receive thrombolytic therapy (73.1 versus 77.8%, P = 0.621), but were less likely to receive revascularisation (29.5 versus 65.1%, P<0.0005) compared with patients <75 years old. We observed a trend towards lower in-hospital mortality for older patients who were revascularised (4.5 versus 7.5%, P = 0.084), an observation not shared by the younger patient cohort (2.3 versus 2.5%, P = 0.82). The great reduction in in-hospital mortality of our older patients over the latter two time intervals, from 30.9% in 1989–1991 to 15.4% in 2001–2002, could possibly be related to the increasing and judicious use of reperfusion, revascularisation and evidence-based medical therapy.

The decline in the incidence of heart failure over the three time periods paralleled the decline in mortality.

Clinical outcome of older patients

Non-ST-elevation acute coronary syndromes

Unlike the case of STEMI, the diagnosis of NSTEMI has changed since year 2000 with the use of the cardio-specific and sensitive troponin markers [16]. This means that more patients diagnosed as unstable angina in the 1980s would now be diagnosed as NSTEMI (with positive troponin), making the interpretation of change in mortality over the years difficult.

Cardiac risk factors

In the two earlier periods, dyslipidaemia was based solely on patient’s history, and routine cholesterol checks were not routinely recorded. In the period 2001–2002, every patient had fasting cholesterol measured, with dyslipidaemia defined as having a total fasting cholesterol of ≥5.5 mmol/l. The Adult Treatment Panel-I (ATP-I) [17], published in 1988, first recommended targeting high low-density lipoprotein (LDL) cholesterol (4.1 mmol/l) or borderline elevated LDL cholesterol (3.4–4.1 mmol/l) in patients with two or more cardiac risk factors for primary prevention for coronary artery disease. In 1994, ATP-II [18] stressed the importance of aggressive LDL reduction for patients with established coronary artery disease, setting a LDL target of <2.6 mmol/l. ATP-III [19], published in 2001, emphasised the need for primary prevention in patients with multiple cardiac risk factors including metabolic syndrome, aiming for an LDL target below 2.6 mmol/l. Improved lipid screening and lower treatment thresholds would account for the more prevalent diagnosis of dyslipidaemia in the period 2001–2002.

The reduction over the years in the proportion of patients with BP ≥140/90 mmHg early after presentation was interesting. This probably reflected better primary and secondary hypertension screening and treatment, but was also relevant in patients receiving fibrinolysis as the complication of intracranial bleeding is definitely related to blood pressure control [20].

Late presentation

Patients were not arriving earlier for medical treatment over the three decades in Dunedin. In The Worcester Heart Attack Study [21], there was also no consistent change in the arrival time of patients presenting to hospital with acute myocardial infarction from 1986 to 1997. It is worth noting that older age was not related to a later presentation. The decline in hospital mortality in STEMI and ACS observed in this study cannot be attributable to earlier hospital presentation.

Our finding of a gender difference in arrival time was interesting. This is becoming more relevant nowadays because of the increasing proportion of older female presenting with ACS. McSweeney et al. [22] found that 95% of women experienced prodromal symptoms (unusual fatigue, sleep disturbances and shortness of breath) 1 month before their ACS, but a significant proportion (43%) of women do not experience the classical symptoms during acute myocardial infarction. This could partly explain why women present later. In contrast, patients with a history of ischaemic heart disease may more correctly interpret their symptoms and present earlier.
Limitations
As in all CCU registry studies spanning long time intervals, admission policies to the CCU and management of ACS would have changed considerably during this study period. Likewise, human longevity also increased significantly. In New Zealand, the median age of death for men and women was 69.5 and 75.3 in 1979, 71.7 and 77.8 in 1989, and 75.0 and 81.3 in 2001, respectively (figures published by Statistics New Zealand). The relatively low number of elderly patients in the first cohort could in part be related to these factors, while multiple non-cardiac co-morbidities in the older patients might also have precluded their admission onto the CCU for ACS. Although this selection bias was to a certain extent inevitable in all CCU registries, an advantage is that the patients studied represented a more homogeneous group with ACS as the predominant problem.

Conclusion
In the past three decades, a higher proportion of older patients were treated in the CCU. Despite that, there has been a definite decline in hospital mortality and heart failure complication for patients with ACS, particularly in older patients and patients with STEMI.

Key points
- This study highlights the rising number of older patients treated in the CCU over three decades.
- Despite that, in-hospital mortality for acute coronary syndrome has declined significantly.
- In-hospital mortality for STEMI in the older (≥75) age group dropped from >30% in the years 1979–1981 and 1989–1991 to 15.4% in the years 2001–2002.

Conflict of interests
No conflict of interest exists.

Acknowledgements
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Informed consent
This registry study was conducted in accordance with the research guidelines approved by the Dunedin Public Hospital at the time of the study.

References
18. National Cholesterol Education Program. Second report of the expert panel on detection, evaluation, and treatment of


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