The Association between Hospital Department, Medical Treatment and Outcome in Acute Myocardial Infarction

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Abstract

Background: Although the preferred management of a patient presenting with an acute myocardial infarction is in a coronary care unit, data based on discharge diagnoses in Israel indicate that many of these patients are treated outside of such units.

Objectives: To compare the demographic and clinical characteristics, treatment and mortality of AMI patients treated inside and outside a CCU.

Methods: We compiled a registry of all patients admitted to three general hospitals in Haifa, Israel during January, March, May, July, September and November 1996.

Results: The non-CCU admission rate was 22%. CCU patients were younger (61.6 vs. 65.5 years), less likely to report a past AMI (18% vs. 34%), and arrived earlier at the emergency room. Non-CCU patients were more likely to present with severe heart failure (30 vs. 11%). Non-CCU patients received less aspirin (81 vs. 95%) and beta-blockers (62 vs. 80%). Upon discharge, these patients were less frequently prescribed beta-blockers and cardiac rehabilitation programs. CCU-treated patients had lower unadjusted mortality rates at both 30 days (odds ratio = 0.35) and in the long term (hazards ratio = 0.57). These ratios were attenuated after controlling for gender, age, type of AMI, and degree of heart failure (OR = 0.91 and HR = 0.78, respectively).

Conclusions: A relatively high proportion of AMI patients were treated outside a CCU, with older and sicker patients being denied admission to a CCU. The process of evidence-based care by cardiologists was preferable to that of internists both during the hospital stay and at discharge. In Israel a significant proportion of all AMI admissions are initially treated outside a CCU. Emphasis on increasing awareness in internal medicine departments to evidence-based care of AMI is indicated.

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Acute myocardial infarction is a leading cause of morbidity and mortality in Israel [1] and the western world [2]. It is believed that part of the decline in coronary artery disease mortality over the last 10–15 years is attributable to new treatments and their availability [3]. The customary management of a patient presenting with AMI includes admission to a coronary intensive care unit, which is accepted as the optimal site for patient monitoring and delivery of care [4]. However, CCU beds are a limited and expensive resource [5].

The decision of whether to admit to the CCU or to an alternative department (usually an internal medicine ward) is based on the patient's clinical characteristics as well as on logistic considerations such as availability of a CCU bed [6]. Indeed, clinical criteria for referral of low risk patients to alternative and less costly admission units are constantly being suggested [7]. Nevertheless, there is an imbalance regarding the admission to CCU for some demographic groups – such as women and the elderly – that might affect prognosis [8–10].

Although the total number of CCU beds in Israel has increased [11], data based on discharge diagnoses of 80% of Israeli hospital admissions (1994–95) showed that almost half the AMI patients were initially admitted outside a CCU [12]. From 1997 to 2000 the situation was little changed. The purpose of this study was to compare the demographic and clinical characteristics, treatment patterns and mortality of AMI patients treated in a CCU with those treated in an internal medicine ward.

Patients and Methods

Patients

All AMI patients younger than 75 years admitted to the three general hospitals in Haifa during January, March, May, July, September and November 1996 were included in the Israel Center for Disease Control AMI registry. Cases were identified by "hot" pursuit (identification and data collection during their hospitalization) and by "cold" pursuit (identification of missed cases and completion of data collection by abstracting information from hospital records and death certificates). We used the MONICA classification of definite AMI for case definition [13]. Briefly, AMI cases met one of the following criteria:

- Definite electrocardiograph (development in serial records of a diagnostic Q wave or an ST segment elevation lasting more than 1 day plus T wave progression)
- Suggestive symptoms together with dynamic ECG (dynamic ST or T changes not sufficient for a definite ECG classification) and abnormal cardiac enzymes (>twice the upper normal bounds of creatine phosphokinase or an abnormal CPK-MB level)

AMI = acute myocardial infarction
CCU = coronary care unit
OR = odds ratio
HR = hazards ratio

CPK = creatine phosphokinase

- Typical cardiac symptoms together with abnormal enzymes and ECG evidence of ischemia, or non-codable ECG (e.g., left bundle branch block) or absent ECG.
- Fatal cases with pathologic diagnosis of AMI (an exceedingly rare category as few autopsies are done in Israel).

Follow-up

A mortality follow-up was done by linkage with the national population registry.

Study variables

Cardiology (non-CCU) departments were grouped with the CCU wards. A patient was considered to be treated in a CCU if admitted to the CCU directly from the emergency room or from another ward within 24 hours of admission, or following new symptoms or ECG changes. Sociodemographic data and clinical history were collected from patients by interview. Missing data were abstracted from patient records. Clinical variables regarding presentation, medications and clinical course were abstracted from the medical records.

Data processing

Statistical analysis was done using SPSS software. Student's *t*-test was used for comparison of continuous variables and the chi-square test for comparing categorical variables between groups. Odds ratios and 95% confidence intervals were used for the comparison of mortality rates. Adjustment for co-variates was done using logistic or linear regression as appropriate or the Mantel-Haenszel procedure. Cox regression was used for survival analysis.

Results

A total of 372 definite AMI patients was identified during the study period. Of the 360 with available information regarding admitting wards, 282 (78%) were admitted directly to a CCU or were transferred to a CCU within 24 hours of admission or appearance of symptoms. The rest were managed in an internal medicine ward. Table 1 shows the demographic characteristics of the patients, and their medical history. CCU patients were younger; the higher male to female ratio among CCU patients reflects the different age distribution among male and female patients. IM ward patients were significantly more likely to have suffered a previous AMI even after adjustment for age and gender.

The groups differed in the characteristics of the event. Eighty-one percent of CCU patients arrived at the emergency room within 12 hours of onset of symptoms vs. 68% of IM ward patients (P = 0.01). More CCU patients received their initial treatment by a mobile intensive care unit (36% of CCU vs. 17% of IM ward patients, P = 0.03). High grade congestive heart failure on presentation (Killip class 3 or 4) was significantly more frequent among IM ward-treated patients (30%) than among CCU patients (11%, < 0.01). Forty-seven percent of the CCU patients were classified as Q wave MI vs. 18% of the IM ward patients (P < 0.01 after adjustment of age and gender).

IM = internal medicine

Table 1. Characteristics of AMI patients by treating ward

	Internal medicine ward (n=78)	Coronary care unit (n=282)	*P* value unadjusted	*P* value adjusted*
% Males	68	78	0.07	0.31**
Age (Mean SD)	65.5	61.6	**<0.01**	**<0.01*****
Past AMI (%)	34	18	**0.04**	**0.04**
Diabetes mellitus (%)	31	23	0.13	0.38
Hypertension (%)	55	44	0.10	0.34
Hyperlipidemia (%)	36	32	0.54	0.56
Smoking (%)	24	40	**0.02**	0.18

* Age and gender adjusted.
** Only age adjusted.
*** Only sex adjusted.
Between 10 and 14% missing values.

Regarding in-hospital medications and after adjusting for age and CHF on admission, patients treated in the IM ward received significantly less aspirin (81 vs. 95%, P < 0.01), beta-blockers (62 vs. 80.0%, P < 0.01) and angiotensin-converting enzyme inhibitors (55 vs. 65%, P = 0.07) than CCU patients. The former underwent less in-hospital angiography (15 vs. 25%) and angioplasty (7 vs. 14%) than CCU patients, although these latter differences were not statistically significant after controlling for age and CHF on admission. Only two IM ward-treated patients received thrombolytic treatment. Discharge recommendations [Table 2] for aspirin, beta-blockers, ACE inhibitors, cholesterol-lowering agents and exercise tests were prescribed less frequently for IM ward patients, although none reached statistical significance. A cardiac rehabilitation program was recommended for 13% of these patients vs. 32% of CCU patients (P = 0.04).

We further examined whether treatment by cardiologists at any stage during the hospital stay might have influenced discharge recommendations. For at least a day during their admission, 303 patients were under the care of cardiologists (both in CCUs or non-CCU cardiology units) and 57 patients were under internist care only. Prescription rates for all of the above evidence-based treatments or tests were lower for patients treated by internists; the difference was significant for beta-blockers (33 vs. 63%, P = 0.01, adjusted for age and CHF on admission) and referral to a cardiac rehabilitation program (5% by internists and 32% by cardiologists, P < 0.01, after adjustment for age and CHF on admission).

Mean length of stay (10 days) did not differ significantly between wards, with a trend towards longer stays among CCU patients (medians of 9 and 7 days among CCU and IM ward patients, respectively).

Mortality data were available for 353 cases (98%). Early and late mortality rates differed significantly between the treating departments. Early (30 day) crude mortality rates in CCU compared with IM ward-treated patients were 7.2 vs. 18.4% (OR 0.35, 95% CI 0.16–0.72). Among patients below age 65 these rates were 3.5 and 11.1% (OR 0.29, 95%CI 0.06–1.28), and for patients aged 65 years or

CHF = congestive heart failure
ACE = angiotensin-converting enzyme inhibitors
CI = confidence interval

Table 2. Discharge recommendations by treating ward and physician's specialty (% of patients)

	Internal medicine ward	CCU	*P* value*	Internists only	Cardio-logists	*P* value*
Exercise test	15	15	0.88	14	15	0.98
Cardiac rehabilitation	13	32	**0.04**	5	32	**<0.01**
Aspirin	74	81	0.74	70	81	0.90
Beta-blockers	45	62	0.19	33	63	**0.01**
Cholesterol-lowering agents	13	18	0.73	12	18	0.61
ACE inhibitors	46	50	0.72	47	50	0.63

* Adjusted for age and CHF (Killip class on admission).

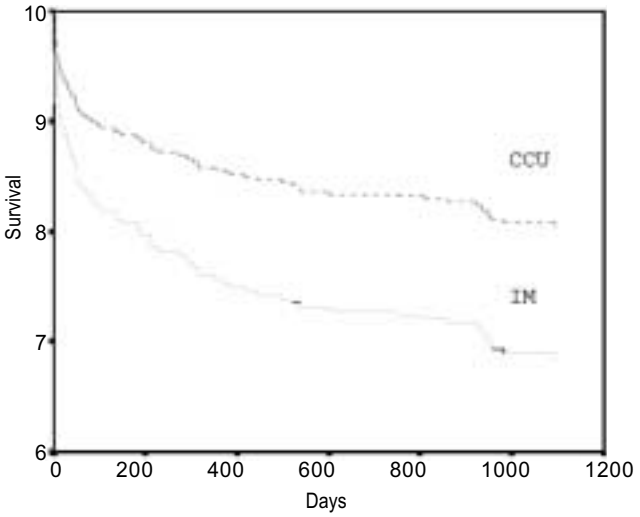

Figure 1. Long-term survival in CCU vs. internal medicine ward-treated patients (in days), adjusted for age (CCU = Coronary care unit, IM = Internal medicine ward).

older, 11.3 and 22.9% (OR 0.43, 95% CI 0.18–1.01). Median follow-up time was 1,032 days. Figure 1 demonstrates the long-term survival advantage for the CCU-treated patients (hazard ratio 0.57, 95%CI 0.36–0.90), adjusted for age. Univariate analysis of early (30 day) mortality found a significant effect for age (OR 2.76, 95%CI 1.40–5.49 for age ⩾65 vs. age <65), and heart failure on presentation (OR 7.41, 95%CI 4.26–12.99 for Killip 3-4 vs. Killip 1-2). In a multivariate analysis containing the above variables as well as the treating ward (CCU vs. IM ward), Q wave vs. non-Q wave myocardial infarction, gender and time from symptom onset to admission, only heart failure remained statistically significant (OR 12.25, 95% CI 4.49–33.40 for Killip 3-4 vs. Killip 1-2), while the CCU effect became attenuated (OR 0.91, 95%CI 0.33–2.54 for CCU vs. IM ward). Table 3 shows the results of Cox regression analysis for long-term mortality. Again, treatment in an internal medicine ward, older age and more severe CHF on admission were associated with increased mortality, whereas Q wave MI and prescription of beta-blockers were associated with reduced mortality. Upon adjustment for these variables the increased risk in patients treated in an IM ward versus CCU, strongly evident in univariate analysis, was attenuated.

We further assessed determinants of long-term mortality excluding in-hospital deaths. In a multivariate analysis including the variables listed in Table 3, the only significant predictors of mortality were older age (HR 3.33, 95%CI 1.67–6.68, for age ⩾ 65 vs. younger) and more severe CHF class on admission (HR 3.63, 95%CI 1.95–6.76, for Killip grade 3-4 vs. 1-2).

Discussion

We have presented the clinical features as well as survival of *all* AMI patients admitted during the study period that were collected through a laborious comprehensive and standardized methodology. The 22% of AMI patients treated in internal medicine departments is lower than reported in other Israeli studies. Rotstein et al. [14] published data based on discharge ICD-9 codes of a single hospital in the Tel Aviv area in 1994–97 and found that 32.7% of AMI patients were managed in an IM ward. Preliminary data from the Acute Coronary Syndrome in Israel Study (ACSIS 2000) report this rate to be 34% for AMI occurring in Israel over a 2 month period in 2000 [15]. This is probably an underestimate since not all IM wards in the country participated whereas all the CCUs were included. A thrombolytic era study from Ireland (using MONICA criteria to validate the diagnoses) found a 30% non-CCU admission rate [16]. Our upper age limit of 75 might explain the lower proportion in our study compared to other Israeli studies. Another determinant of importance is the fact that some of the patients admitted initially to an IM ward are later transferred to a CCU, a factor taken into account in our study but difficult to capture in a cross-sectional survey, such as ACSIS 2000. Older AMI patients tend to be triaged away from the CCU. This age discrimination has been noted in large clinical trials [17]. We also found women to have a lesser chance of admission to the CCU. The older age of women in this registry explains part of the difference, but data from the Israel Ministry of Health central patient registry showed lower CCU admission rate for women than men in all age groups [12].

Patients treated in an internal medicine ward had more severe coronary disease as evidenced by a higher percentage of previous AMI and of heart failure on admission that persisted after adjustment for age, indicating increased risk in this group.

Table 3. Univariate and two multivariate analysis models of long-term mortality*

	Univariate	Multivariate I	Multivariate II
CCU vs. Non-CCU	0.47 (0.30– 0.74)	0.75 (0.46–1.23)	0.78 (0.47–1.28)
Men vs. women	0.70 (0.45–1.09)	1.17 (0.72–1.91)	1.06 (0.64–1.73)
Age ⩾ 65 vs. age <65	3.33 (2.08–5.34)	2.67 (1.56–4.57)	2.28 (1.32–3.93)
Q wave vs. non-Q wave	0.58 (0.37–0.92)	0.81 (0.48–1.36)	0.85 (0.50–1.42)
Killip 3-4 vs. Killip 1-2	6.76 (4.44–10.30)	5.00 (3.07–8.15)	4.44 (2.71–7.26)
Discharge beta-blockers vs. none	0.30 (0.19–0.46)		0.49 (0.30–0.79)

* Cox regression analysis. Data shown are hazards ratios.

Late arrival can be a contraindication to thrombolysis and thus may affect mortality. Indeed, there were significant differences between the groups: although most of the patients arrived within the thrombolytic window time of 12 hours, more CCU than IM ward patients did so (81 vs. 68%). A greater proportion of care by mobile intensive care unit among CCU patients suggests earlier administration of efficacious treatment in this group [18]. More IM ward-treated patients were in Killip CHF classes 3 or 4. For a patient with these Killip categories there was a threefold greater probability of being admitted to an internal medicine department. In a recent Israeli survey of patients younger than 65 in eight major hospitals among [19], the likelihood of referral to an IM ward (compared with CCU) increased stepwise with the increasing number of a patient's predictive factors: advanced age, history of hypertension or diabetes, a longer time from appearance of symptoms to arrival at the hospital, and myocardial infarction type (non-Q wave or non-anterior). Why were more severe patients directed to an IM department and other patients preferred in the competition for CCU beds? Might the triage physician have considered some of these patients to have such a grave prognosis that CCU admission was futile? There may also be other unmeasured characteristics that might have influenced the decision, such as poor functioning category, dementia, or other terminal illnesses.

Patients treated in an IM department were given less aspirin, ACE inhibitors and beta-blockers than those treated in a CCU and were prescribed less beta-blockers and cardiac rehabilitation programs at discharge. This may result from differences in medical knowledge of the treating physicians (cardiologists versus internists) and/or to more contraindications for these medications among the medicine ward patients. Ayanian et al. [20] surveyed 1,211 cardiologists, internists and family physicians in New York and Texas regarding their practices concerning specific drug prescriptions post-AMI. They found that internists prescribed much less aspirin and beta-blockers. Frances and colleagues [21] reviewed 7,663 charts of AMI patients and found significantly less aspirin prescribed by treating internists vs. cardiologists. They also note that this and other prescription differences did not account for differences in outcome. Although the benefits of aspirin, ACE inhibitors and beta-blockers were already well known, our study was carried out at the time data were published on the efficacy of beta-blockers in CHF after AMI [22].

CCU-treated patients had better age and gender-adjusted survival. This may be explained by more appropriate treatment in the CCU or at discharge, by the fact that the IM ward patients were sicker at admission regardless of the treatment that was given (case mix), or both. As discussed previously the process of care provided by cardiologists was better than that of the internists. In light of the strong association of beta-blockers recommended at discharge with prognosis, use of this drug may be viewed as a surrogate marker for a better process of care. Variables besides the treating department that influenced mortality were older age, non-Q wave AMI, CHF on admission and non-prescription of beta-blockers. All these variables were more prevalent among the internal ward patients. Combining these parameters in a multivariate analysis we found only CHF, old age and non-use of beta-blockers to be statistically significant predictors of higher mortality. The effect of the AMI type (Q vs. non-Q wave) on mortality was confounded by age, degree of CHF, and treating department. The substantial effect of CHF at admission on prognosis persisted after adjustment, pointing to its importance regardless of age, type of AMI or treating department. Results from the ACSIS 2000 [15] compared to this registry suggest a relatively poorer 30 day prognosis for CCU patients (9.2% mortality rate vs. 7.2% in our study) but a slightly better outcome for internal medicine ward patients (15.5% mortality rate vs. 18.4% in our study). The differences, within the bounds of chance, may be influenced also by differences in age and AMI definitions, i.e., MONICA criteria vs. a clinical diagnosis. Adjustment for age, AMI type, CHF and co-morbidity largely abolished both early and late mortality rate differences between patients in our study treated in the CCU and the IM ward. Given the high proportion of AMI patients admitted to an IM ward, this is an issue of major importance in Israel and other European countries where admission to internal medicine departments is frequent.

This study is not without limitations. Some variables could not be validated. For example, CHF on admission was based only on the admitting physician's examination and some cases may have been missed. Nevertheless, the prolective collection of data coupled with the retrolective abstraction of information from patients' files using a uniform protocol [13] render these results comparable to other similar studies around the world [23]. Recently, Tunstall-Pedoe and colleagues [24] estimated the contribution of changes in coronary care to survival from coronary disease across 31 MONICA populations. They found that changes in coronary care as evidenced by increasing rates of prescription of evidence-based treatments before, during and after the infarction were strongly linked with better survival. Thus, this uniformity in methodology not only forms the basis for comparison of the quality of care between centers and countries, but it also allows for the detection of secular changes regarding coronary disease event rate, mortality, quality of care and their determinants. Perry et al. [25] evaluated the costs and benefits of four alternative monitoring systems for coronary heart disease in Scotland: a community epidemiology model based on MONICA methodology, models based on the Australian cardiovascular disease monitoring scheme, and on enhanced routine data and a coronary heart disease registry modeled on the Scottish Cancer Registry scheme. They concluded that the most beneficial monitoring system is the community epidemiology model based on MONICA study methodology.

In conclusion, a substantial proportion of patients were admitted to internal medicine departments where acute coronary care is suboptimal. Furthermore, patients with a poorer prognosis were more likely to be admitted to an IM department. Upon multivariate adjustment for severity, no differences in long-term survival was evident between CCUs and IM departments. Nonetheless, efforts should be made both to upgrade care in medicine departments and to ensure that CCUs serve their primary purpose, i.e., that non-admission to a CCU should be the exception rather than a frequent practice. However, due to the high cost of adding CCU beds, and the continuing role of CCUs in salvage of patients undergoing invasive procedures, it is likely that a substantial

proportion of AMI patients will continue to be admitted to internal medicine wards in Israel. The question is whether the gap in simple evidence-based care can be eliminated between cardiologists and internists, and between CCUs and medicine departments, by focussed interventions among internists directed to adherence to published guidelines. Quality assurance measures should be established in each hospital to verify that this goal is achieved.

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Capsule

Cooperative fibril formation

Many neurodegenerative diseases are characterized by the formation of pathologic intraneuronal inclusions containing fibrils of polymerized proteins. For example, tau fibrils constitute the neurofibrillary tangles characteristic of Alzheimer's disease, and alpha-synuclein fibrils are the principal constituent of Lewy bodies, the pathologic hallmark of Parkinson's disease. Giasson and co-workers now show that alpha-synuclein can induce the tau protein to form fibrils and that, when co-incubated, these two proteins can induce fibrillization of each other.

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