Stenting in Acute Myocardial Infarction: in Hospital and Long-Term Follow-Up

Nethaniel Horowitz MD[1], Michael Kapeliovich MD PhD[2], Rafael Beyar MD DSc[3] and Haim Hammerman MD[2]

[1] Department of Internal Medicine D, [2]Intensive Cardiac Care Unit and [3]Interventional Cardiology Unit, Department of Cardiology, Rambam Medical Center, Haifa, Israel
Affiliated to Technion Faculty of Medicine, Haifa, Israel

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Abstract

Background: Coronary stenting was recently introduced as a primary intervention for acute myocardial infarction. Several randomized controlled studies have shown that stenting may be superior to balloon angioplasty for the treatment of AMI. However, routine stenting may also cause deterioration of coronary flow.

Objective: To analyze the clinical characteristics and the outcome of patients who were treated with stenting for AMI in our center in the recent era of stenting.

Methods: Fifty-five patients with AMI were treated by stent implantation between January 1998 and December 1999. Adverse clinical events were recorded, including death, recurrent infarction, coronary artery bypass grafting, cerebrovascular accident, and target vessel revascularization. In-hospital, 1 month, 6 month and 1 year follow-up was performed in all patients. Repeat coronary angiography was performed according to clinical indications.

Results: Baseline angiographic results showed Thrombolysis in Myocardial Infarction (TIMI) 0 flow in 39 patients (70.9%), TIMI I flow in no patient and TIMI II/III flow in 16 patients (29.1%). TIMI grade 3 flow was achieved in 90.9% of patients at the end of the procedure. In-hospital mortality rate was 5.4% (2.1% in patients without cardiogenic shock). There was no evidence of re-infarction or TVR. The rates of bleeding complication (all of them minor), CVA, and CABG were 9.1%, 3.6% and 1.8% respectively. The 6 month mortality rate remained the same. Rates of re-infarction, restenosis, TVR and CABG were 3.6%, 14.5%, 14.5% and 5.4% respectively. The 1 year mortality rate was 7.3%. Restenosis rate was 18% and CABG 7.3%. One year event-free survival was 70.9%.

Conclusions: This study suggests that stenting is a safe and effective mode of therapy in the setting of AMI associated with a high rate of revascularization and a low short and long-term outcome.

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Myocardial infarction generally occurs when there is an abrupt decrease in coronary blood flow following a thrombotic occlusion of a coronary artery, previously narrowed by an atherosclerotic plaque. After an initial platelet monolayer is formed at the site of the ruptured plaque, a variety of agonists promote platelet activation. The coagulation cascade is also activated on exposure of tissue factor in damaged endothelial cells at the site of the plaque. The culprit coronary artery eventually becomes occluded [1]. It is common practice today that timely administration of thrombolytic therapy after coronary arterial occlusion (in ST elevation acute myocardial infarction) results in myocardial salvage and improves survival [2]. The major advantage of thrombolysis lies in its wide applicability to patients in different clinical settings (ambulances, emergency rooms, critical care units, etc.). However, the major limitation of thrombolysis is hemorrhagic complications and relatively low rates of TIMI grade 3 flow. To overcome these inherent limitations of thrombolytic therapy, new modes of reperfusion for AMI are currently being evaluated.

Percutaneous transluminal coronary angioplasty in AMI is an excepted alternative to thrombolysis [3]. It has been shown to result in lower rates of mortality, recurrent AMI and stroke. However, there are several limitations to this method of reperfusion. Dissection, restenosis, reocclusion, and the need for re-intervention remain significant challenges [4]. The mechanism of reocclusion of the infarct-related vessel may be instability of the underlying plaque itself [5]. Other mechanisms are: an increased tendency of plaque dissection and rupture [6], and a high level of platelet activation during percutaneous transluminal coronary angioplasty in AMI [7].

Coronary stent implantation has reduced the rate of thrombotic and restenotic events as compared to plain PTCA [8]. Thus coronary stent placement through its mechanical scaffolding properties and improvement in flow characteristics, combined with the effects of subsequent antiplatelet therapy, has the potential of stabilizing the plaque of the infarct-related artery [9]. At the beginning of the stenting era there was concern that stents may be detrimental in a thrombus-rich environment such as AMI.

Several randomized controlled trials have compared stenting of infarct-related artery with plain balloon angioplasty for the treatment of AMI, and showed the safety and feasibility of this method [10–14]. While benefits for stents over balloon angioplasty could be shown in some studies, there is still concern about the results of stenting and PTCA in a "real world" practice, and whether they are comparable to those achieved in randomized trials. Therefore, the goals of the present study were:

AMI = acute myocardial infarction
TVR = target vessel revascularization
CVA = cerebrovascular accident
CABG = coronary artery bypass grafting

TIMI = Thrombolysis in Myocardial Infarction
PTCA = percutaneous transluminal coronary angioplasty

- To analyze short and long-term clinical results of primary coronary intervention using stents in patients with AMI, in a single, large-volume university hospital.
- To compare the results with those obtained from randomized and non-randomized trials.

Methods

Between 1 January 1998 and 31 December 1999, primary PTCA was performed in 62 patients admitted with the diagnosis of AMI within 12 hours from onset of chest pain. Stent implantation was attempted in 55 patients, all of them successfully. The reasons to avoid stenting in seven patients were acute thrombosis of previous stent in the infarct-related artery (four patients), major side branch jeopardy (two patients), and a small infarct-related artery with lumen diameter less then 2.5 mm (one patient).

Indications for reperfusion therapy were based on the following criteria:

- Typical ischemic chest pain, lasting longer than 30 minutes, within 12 hours from symptom onset.
- Electrocardiographic ST segment elevation of 0.1 mV in two contiguous leads.

The diagnosis of myocardial infarction was confirmed by elevation of serum total creatinine phosphokinase and its MB isoenzyme to at least twice the upper limit of normal. The decision to perform primary percutaneous coronary angioplasty instead of thrombolysis was based on the following criteria:

- Large anterior or non-anterior AMI.
- Hemodynamic instability in a patient with AMI.
- Contraindication to thrombolytic therapy.
- AMI in the territory of previously stented artery.
- Availability of experienced personnel in a reasonable time period.

Indications for coronary stenting were:

- Suboptimal angiographic result after angioplasty.
- Coronary artery dissection of any type.

Before the intervention, patients received aspirin. Heparin was administered by bolus and continued infusion after the procedure, and for at least 12 hours. Subsequently, all patients received aspirin. Ticlopidine was given for 3 weeks. Abciximab or eptifibatide infusions were given according to the clinical decision of the operator in charge.

The concomitant treatment and follow-up was left to the decision of the attending cardiologist, and according to the American Heart Association/American College of Cardiology recommendations [15].

After discharge, the protocol included contact by phone, or at our outpatient clinic at 30 day, 6 month and 1 year periods. A record was made of any hospitalization or adverse event for all the patients. Detailed in-hospital, 1 month, 6 month and 1 year follow-up case report forms were prospectively completed for each patient. Angiographic follow-up was performed only in patients with clinical indications. Clinical and angiographic data were entered into a computerized database, and statistical analysis was performed with STAT CALC from EpiInfo 5 and SPSS commercial software.

Definitions

Outcomes of this prospective study were: in-hospital, 1 month, 6 month and 1 year rate of adverse clinical events including: death of any cause, AMI, CABG, TVR, CVA (in-hospital only), and restenosis (angiographically proven). Discrete data are summarized as frequencies, while continuous data as mean $\pm$ SD. Estimate of event-free survival was determined using the Kaplan-Meier method. Comparison between our results and others was performed using one-tailed Z test for comparison of two proportions or Fisher's exact test.

Results

Baseline clinical, demographic and angiographic characteristics are shown in Table 1. Men comprised 75.4% of the patients. The mean age was 59 $\pm$ 12.37 years (range 37–81 years); 12.7% of the patients

Table 1. Baseline clinical and angiographic characteristics

	No	%
Men	41	74.5
Women	14	25.5
Age (yr)	59	$\pm$12.37
Hypertension	18	32.7
Diabetes mellitus	18	32.7
Family history of CAD	17	30.9
Smoking	34	61.8
Hypercholesterolemia	19	34.5
Hypertriglyceridemia	2	3.6
Prior angina pectoris	17	30.9
Previous MI	14	25.5
Previous CABG	0	0.0
Previous PTCA in infarct-related artery	5	9.1
Previous stent in infarct-related artery	2	3.6
Infarct-related artery		
LAD	40	72.7
RCA	13	23.6
LCX	2	3.6
Extent of coronary disease		
1-vessel disease	18	32.7
2-vessel disease	22	40.0
3-vessel disease	15	27.3
Localization of MI		
Anterior	42	76.4
Non-anterior	13	23.6
Kilip class on admission to cath lab		
1	37	67.3
2	9	16.4
3	3	5.5
4	6	10.9
TIMI flow on the first coronary injection		
0	39	70.9
1	0	0
2	7	12.7
3	9	16.4

were 75 years or above. There was a 32.7% incidence of hypertension and 32.7% had diabetes mellitus. The incidence of family history of ischemic heart disease was 30.9%, and 61.8% were smokers. The incidence of prior angina pectoris was 30.9% and of hypercholesterolemia 34.5%. More then half of the patients had anterior AMI (76.4%) and 10.9% had cardiogenic shock on admission. Non-ST elevation AMI was diagnosed in five patients (9.1%). The infarct-related artery was left anterior descending in 72.7% of patients, right coronary artery in 23.6%, and left circumflex artery in 3.6%.

Stents were successfully placed in 55 patients. Technical success was 100%. Successful opening of the infarct-related artery with TIMI 3 flow at the end of the procedure was achieved in 50 patients (90.9%), TIMI 2 flow in 1 patient (1.8%), TIMI 1 flow in 3 patients (5.5%), and TIMI 0 flow in 1 patient (1.8%).

In-hospital results

During index hospitalization the overall mortality was 5.5%. Mortality was 2.1% in the patients with cardiogenic shock and 25% in patients with cardiogenic shock. There was no re-infarction during hospitalization. Subacute coronary occlusion was suspected in one patient (1.8%) but was not proved by angiography. One patient underwent emergent CABG 1 day after stenting because of development of ventricular-septal defect (1.8%). Two patients suffered ischemic CVA (3.6%). Bleeding complications were detected in five patients (9.1%) and were all minor [Table 2]. Two patients were treated with abciximab and one patient with eptifibatide.

Long-term follow-up

At 1 month there was no evidence of additional death, non-fatal re-infarction, restenosis or TVR in our study population. At 6 months follow-up there was no additional death. There were two episodes of non-fatal re-infarction. Eight patients suffered from restenosis and underwent revascularization of the infarct-related artery. An additional patient underwent CABG. Data for 1 year follow-up were available for all patients. There was an additional death (at 10 months), two patients underwent CABG, and there were two additional cases of stent restenosis. There was no case of TVR or re-infarction in this period [Table 2]. Event-free survival rate at 1 year was 70.9%.

Discussion

Coronary stent implantation in AMI has reduced the rate of thrombotic and restenotic events in comparison with PTCA [10–14]. Nonetheless, there is still concern about the results of stenting in AMI in a "real world" practice and whether they are comparable to those achieved in previous randomized trials. The current study shows that primary PTCA with stenting is safe in AMI. TIMI grade 3 flow was achieved in 90.9% of patients. In-hospital mortality rate was 5.4% (in patients without shock, 2.1%). The rates of bleeding complication, CVA, and CABG were 9.1%, 3.6%, and 1.8% respectively. At 6 months the mortality rate remained the same. The 1 year mortality rate was 7.3%. Restenosis rate was 18% and CABG 7.3%.

Table 2. In-hospital and long-term clinical outcomes

In-hospital outcomes	No. of events	(%)
Death	3	5.5
Death in patient with cardiogenic shock (n=8)	2	25
Death in patient without cardiogenic shock (n=47)	1	2.1
Re-infarction	0	0
TVR	0	0
CABG	1	1.8
Bleeding complications	5	9.1
CVA	2	3.6
ICCU stay (days)	5.5	
Hospital stay (days)	12.5	
1 month		
Death	3	5.5
Re-infarction	0	0
Restenosis	0	0
TVR	0	0
CABG	1	1.8
CVA	2	3.6
6 months		
Death	3	5.5
Re-infarction	2	3.6
Restenosis	8	14.5
TVR	8	14.5
CABG	2	3.6
1 year		
Death	4	7.3
Re-infarction	2	3.6
Restenosis	10	18
TVR	8	14.5
CABG	4	7.3

Table 3. Data from randomized controlled studies

Study	Strategy	N	Success (%)	Reocclusion (%)	Death (%)	Recurrent MI (%)	TVR (%)	Follow-up
GRAMI [14]	Stent	52	98	0	3.8	0	0	In hospital
	PTCA	52	94.2	7.7	7.6	7.6	5.7*	
FRESCO [10]	Stent	75	99		0	1	5	6 month
	PTCA	75	100		1	3	17	
ZWOLLE [12]	Stent	112	98	1	2	1	4	6 month
	PTCA	115	96	5	3	7	17	
STENT PAMI [11]	Stent	452	89		4.2	2.4	7.7	6 month
	PTCA	448	93		2.7	2.2	17	
STENTIM-2 [13]	Stent	101	86		3	4.0	16.8	1 year
	PTCA	110	82.7		1.9	5.5	27.3	

* By repeat PTCA only.

We reviewed data from randomized trials that compared primary stenting in acute MI with primary PTCA alone [Table 3]. The number of enrolled patients ranged from 52 to 452. Follow-up ranged from the in-hospital period to approximately 1 year. Procedural success rates were achieved in 86–99% in the stent group and in 82.7–100% in the PTCA group. Mortality rates ranged from 0% to 4.2% in the stent group and 1–7.6% in the PTCA group. Incidence of recurrent AMI was also low, 0–4% in the stent group and 2.2–7.6% in the PTCA group. Rates of TVR by PTCA or by CABG ranged from 0 to 16.8% in the stent group and 5.7 to 27.3% in the PTCA group.

Table 4. Comparison with data from non-randomized similar studies

Study	N	TIMI 3 flow (%)	Reocclusion (%)	Death (%)	Recurrent MI (%)	TVR (%)	Follow-up
Castrati et al.	519	91.5	3.2	5.4	1.2	4	30 days
[16][16]	519			11	3.1	14	1 year
Stone et al.	236	94	1.3	0.8*	1.7	2.1	In hospital
[17][17]	236			2.5	3.8	10.2	6 months
Antoniucci et al.	176	99		6	0	3.4	30 days
[18][18]	176			8	0**	14	6 months
Rambam	55	90.9	1.8	5.4	0	0	30 days
	55			5.4	3.6	14	6 months
	55			7.3	3.6	14	1 year

* $P = 0.047$
** $P = 0.013$

Several prospective series reporting the use of stenting in AMI have been published [16–18] [Table 4]. Our study was compared to these three studies because of similar design. Yet those studies used primary PTCA with stenting as a primary strategy for AMI, while in our work primary stenting was attempted in selected patients with large AMI, or in patients with relative contraindications for thrombolysis. The number of patients in these studies varied from 176 to 519, and follow-up from 30 days to 1 year. TIMI grade 3 rates were high (91.5–99%).

Early mortality rates ranged from 0.8 to 6%. Incidence of early recurrent AMI was also low (0–1.7%). Data of long-term follow-up were similar to our data. Mortality rates were 2.5–11%. Recurrent AMI ranged from 0 to 3.8% and rates of TVR by PTCA from 10.2 to 14% during follow-up.

The early mortality data in our study compare favorably with other data from non-randomized studies [16–18], as well as randomized studies [10–14]. Regarding mortality, it is important to differentiate between patients with and without cardiogenic shock. Most of the randomized studies (except the FRESCO trial) did not enroll patients with cardiogenic shock. For example, the ZWOLLE study enrolled only patients in relatively stable hemodynamic condition. In patients without cardiogenic shock our results are similar to those presented in other studies. The survival data in patients with cardiogenic shock in our series are better as compared to the literature, probably due to the small sample size. The findings in our relatively small series may serve as additional data supporting the beneficial results of the invasive approach in the first hours of AMI.

Recent studies [10–14] have shown that primary PTCA with stent is superior to primary PTCA without stent. In contrast, in the Stent PAMI trial there was a strong trend toward early and late increased mortality in patients with stented infarct-related artery, which was related to diminished TIMI grade 3 flow following stent implantation.

In our institution, primary PTCA with stent implantation is implemented as "tailored therapy" in AMI, i.e., patients with contraindication to thrombolysis or have a large AMI are treated with this method. We believe that by so doing, the maximum benefit of the therapy is achieved.

There are little data on the results of stenting during primary PTCA in a non-selected population of patients with AMI. In our prospective non-randomized study we show that primary stenting can be applied safely in a setting of a tertiary medical center, in a selected group of patients with contraindication to thrombolysis or large AMI. The high incidence of elderly patients (older than 75 years, 12.7%) and of patients with cardiogenic shock (10.9%) was the most relevant characteristic of the population in our study, as compared to those of other randomized studies that excluded high risk patients (e.g., with cardiogenic shock or older than 75 years).

There are limited data on long-term follow up (e.g., 6 and 12 months) of stenting in the setting of AMI. Our results compare favorably with those obtained in randomized and non-randomized studies that deal with long-term follow-up. It is important to stress that although our study enrolled patients with cardiogenic shock (10.9%), this fact did not influence our long-term results. The high incidence of restenosis was significant after 6 months according to clinical date, and eventually decreased significantly. This fact is in agreement with previous observations that, after 6 months, restenosis is not a common occurrence [19].

Limitations

This study includes a consecutive, selected, relatively small series of patients with AMI treated with primary PTCA and stenting. Our main objective was to describe the clinical condition of these patients at presentation, and the early and late outcomes. We compared our results with data from other studies. However, this comparison is not a substitute for controlled randomized studies.

Conclusions

We conclude that primary PTCA and stenting is a safe and effective therapy in a selected group of patients with AMI and carries a favorable short and long-term outcome. Obviously, a primary PTCA program requires a proper catheterization laboratory and hospital organization to allow the proper identification and selection of eligible patients, and to optimize the time to reperfusion between thrombolytic and primary PTCA strategies.

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Correspondence: Dr. N. Horowitz, Dept. of Internal Medicine D, Rambam Medical Center, Haifa 31096, Israel.
Phone: (972-4) 854-2263
Cellular: (057) 673410
email: Nattyh1@hotmail.com

Capsule

Uncertain role of thromboytic therapy for pulmonary embolism

In a recent editorial, Dalen reviewed the meta-analysis performed by Agnelli et al. comparing heparin and thrombolytic therapy in pulmonary embolism (PE). Five years ago, a similar meta-analysis was carried out by Dalen and co-workers which, in sharp contrast, showed that thrombolytics did not reduce PE mortality or recurrence. Differences in outcome were due to four newer trials in which 7/58 patients treated with heparin died as compared with 1/41 patients treated with thrombolytics. However, Agnelli failed to report the gross discrepancies in treatment administration, namely that patients treated with thrombolytics were treated within 4 hours after onset of symptoms compared to an average of 34 hours after onset of symptoms in heparin-treated patients. When comparing PE recurrence, fewer heparin patients were followed with a lung scan, and when comparing confirmed cases, the rates for recurrence were similar (3.3% thrombolytics, 4.5% heparin). In addition, initiation of thrombolytics led to a marked improvement after 24 hours, but 1 week later a lung scan showed no differences between heparin patients and thrombolytic patients.

Other clinical trials have also been inconsistent, possibly due to selection bias, differences in cardiac dysfunction, etc. However, what is clear is that there is more to Agnelli's meta-analysis than meets the eye. Dalen contends that thrombolytic therapy has its applications and should be reserved for patients with massive PE complicated by shock.

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