Although the traditional transfemoral arterial approach (TFA) for catheter-based coronary or carotid intervention is still popular,\(^1\)–\(^4\) it has disadvantages, including the need for bed rest, puncture site compression after the procedure, and vascular complications of hematoma and arteriovenous fistula, as well as difficult access because of the tortuous aorta or if there is occlusion of the femoral-iliac-aortic route.\(^6\)–\(^12\) The transradial arterial approach (TRA), which is a fairly simple route of access\(^13,14\) for catheter-based coronary intervention, has been developed for more than 15 years and since the safety and efficacy of this method was fully discussed and validated,\(^13,15\) it has become a widely used approach, especially in Asia, for elective percutaneous coronary intervention (PCI).\(^15\)–\(^19\) Recent studies have further indicated that TRA is safe and efficacious for elective coronary angiographic studies of outpatients,\(^20\) elective left main coronary intervention,\(^21\) cerebral angiographic studies or vertebral or carotid stenting.\(^22,23\) So currently, the TFA and TRA are the most popular vascular access routes for various types of PCI worldwide, but while the safety and efficacy of the TFA approach for acute myocardial infarction (AMI) patients undergoing primary PCI have been extensively discussed,\(^3,24,25\) relevant issues for using the TRA for primary PCI have not been fully investigated\(^26\) in an era when TRA for primary PCI is already daily practice in some medical centers.\(^27,28\) Therefore, the aim of this study was to elucidate whether initial selection of the TRA was inferior to initial selection of the TFA for AMI patients undergoing primary PCI. However, in the present study, the incidence of combined vascular and bleeding complications was lower with the TRA than with the TFA approach. (\textit{Circ J} 2009; 73: 2050–2055)

**Key Words:** Acute myocardial infarction; Primary percutaneous coronary intervention; Transradial arterial approach
Methods

AMI Patient Population
According to the treatment protocol at Kaohsiung Chang Gang Memorial Hospital, since May 1993 all patients with ST-segment elevation (ST-se) AMI of onset <12 h are eligible for primary PCI. For the purpose of this study, detailed in-hospital and follow-up data, including age, gender, coronary artery disease risk factors, serial creatine kinase (CK) levels, white blood cell (WBC) counts, creatinine levels, body temperature, Killip score on admission and severity of chronic heart failure were collected prospectively and entered into a computer database. The angiographic findings, including collateral circulation and Thrombolysis In Myocardial Infarction (TIMI) flow grades in the culprit coronary artery, lesion length, pre- and post-PCI minimal lumen diameter (MLD) and reference lumen diameter (RLD) were also recorded and entered into the database.

Exclusion Criteria
This study was performed from May 1993 to May 2007. More than 90% of the cardiogenic shock patients received intra-aortic balloon pump (IABP) support via TFA, including 12 patients who received both IABP and extra-corporeal membrane oxygenator (ECMO). Because it is well recognized that patients with AMI complicated by cardiogenic shock always have a poor clinical outcome, such patients were excluded from the current study to avoid a categorized bias that would distort the statistical significance of the clinical outcomes between the TFA and TRA groups. Additionally, since May 2002, AMI patients with high-burden thrombus formation have been enrolled in a mechanical distal protection trial. We recently reported that the PercuSurge GuardWire device effectively prevented distal embolization and markedly improved the integrity of the microvasculature and clinical outcome during primary transradial coronary intervention in AMI patients. Despite a protocol violation, this strategic management actually provided favorable angiographic outcomes. Accordingly, patients with AMI who underwent primary PCI using the PercuSurge distal protection device were excluded from this study.

Procedure and Protocol for TFA
Between May 1993 and February 2002, emergency cardiac catheterization via TFA routinely using a 7-French arterial sheath was performed in 841 patients of all ages presenting with AMI (≤Killip 3 upon presentation) of <12 h duration; 13 (1.6%) of the 841 patients were treated conservatively and excluded because the AMI was caused by either coronary artery spasm (7 patients) or stenosis of the culprit lesion <60% with normal coronary flow (6 patients), resulting in a total of 828 patients undergoing primary PCI. Of them, 18 (2.2%) with either infarct-related mechanical complications or significant left main arterial disease and severe multivessel disease requiring either urgent or emergency surgical intervention after primary PCI were also excluded. The remaining 810 patients comprised the TFA group (ie, Group 2).

The procedure and protocol have been described previously in detail. Before coronary stents were available in Taiwan, primary balloon angioplasty was the procedure of choice, but after the introduction of coronary stents in 1998, primary stenting has become the preferred procedure for most patients.

Procedure and Protocol for TRA
The TRA approach using a 6-French arterial sheath has been routinely used for the treatment of AMI since March 2002 unless the Allen’s test was positive on both sides. A 6-French Kimny Miniradial guiding catheter (Boston Scientific, Scimed, Inc, Maple Grove, MN, USA) was used for both diagnosis and primary PCI.

Between March 2002 and May 2007, emergency cardiac catheterization via TRA was performed in 917 patients of any age with AMI ≤Killip 3 who presented at hospital <12 h after onset; 11 (1.2%) patients were treated conservatively and excluded because the AMI was caused either by coronary artery spasm (6 patients) or stenosis of the culprit lesion <60% with normal coronary flow (5 patients). Of the remaining 906 patients undergoing primary PCI, 7 (0.8%) with either infarct-related mechanical complications or significant left main arterial disease and severe multivessel disease requiring either urgent or emergency surgical intervention after primary PCI were excluded. In addition, 30 (3.3%) of the 899 patients who underwent primary PCI using the TFA were excluded because of either decreased or undetectable radial pulse. Furthermore, 50 (5.8%) of the remaining 869 patients, who later underwent the TFA approach immediately after initiation of IABP support because of an unstable clinical condition upon cardiac catheterization, were also excluded, as were 313 (38.2%) patients who had high-burden thrombus formation requiring primary PCI with the PercuSurge GuardWire device during this study period. As a result, 506 patients served as Group 1 (TRA).

Anticoagulant Usage
Clopidogrel was available in Taiwan only from the late TFA period. Previously, patients undergoing primary coronary stenting were given ticlopidine (500 mg preoperative loading dose, then 250 mg/day) for at least 4 weeks, but after clopidogrel became available, it was administered as a 300-mg preoperative loading dose and then 75 mg/day for at least 4 weeks. Each patient was given chewable aspirin (324 mg) and a 5,000-U bolus of intravenous heparin in the emergency room. Before primary PCI, the patient received intracoronary heparin (5,000–10,000 U) to achieve an activated clotting time (ACT) ≥320 s. Heparin was given continuously to patients who underwent primary balloon angioplasty only (for 48 h), to those whose final TIMI flow was ≥2 in the infarct-related artery (IRA), and to those who had received IABP support. Aspirin (orally 100 mg/day) was given to each patient indefinitely.

Tirofiban, a platelet glycoprotein IIb/IIIa inhibitor, was only used in the late TFA study period because its availability at our hospital was delayed until January 2001. Other commonly prescribed medications were angiotensin-converting enzyme inhibitors, statins, β-blockers, isordil/isosorbidenonitrater, and diuretics.

Usage of IIb/IIIa Receptor Inhibitor
Between May 2001 and April 2003, patients were administered A loading dose of tirofiban (20 μg/kg body weight) upon presentation in the emergency room, followed by a maintenance infusion of 0.15 μg/kg·min⁻¹ for 18–24 h. However, tirofiban therapy was subsequently withheld
Table 1. Baseline Characteristics of AMI Patients

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=506)†</th>
<th>Group 2 (n=810)§</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean±SD)</td>
<td>61.0±12.1</td>
<td>61.5±12.1</td>
<td>0.526</td>
</tr>
<tr>
<td>Male gender</td>
<td>81.6% (413)</td>
<td>84.2% (682)</td>
<td>0.224</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>35.0% (177)</td>
<td>26.1% (211)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Hypertension</td>
<td>56.5% (286)</td>
<td>50.1% (406)</td>
<td>0.237</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>43.2% (216)</td>
<td>39.9% (323)</td>
<td>0.313</td>
</tr>
<tr>
<td>Current smoking</td>
<td>27.3% (138)</td>
<td>53.3% (452)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous MI</td>
<td>4.4% (22)</td>
<td>10.1% (82)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>6.7% (34)</td>
<td>7.0% (57)</td>
<td>0.825</td>
</tr>
<tr>
<td>Killip 3</td>
<td>10.3% (52)</td>
<td>12.6% (102)</td>
<td>0.204</td>
</tr>
<tr>
<td>≤Killip 2</td>
<td>89.7% (454)</td>
<td>87.4% (708)</td>
<td></td>
</tr>
<tr>
<td>AWMI by ECG</td>
<td>59.5% (301)</td>
<td>57.3% (464)</td>
<td>0.431</td>
</tr>
<tr>
<td>Peak CK level</td>
<td>2.21±2.585</td>
<td>3.46±3.304</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pre-infarct angina</td>
<td>14.2% (72)</td>
<td>28.5% (231)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Collateral circulation</td>
<td>14.2% (72)</td>
<td>29.4% (238)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are mean value±SD or % (number) of patients.
*Continuous data were analyzed using t-test and categorical data were analyzed using chi-square test.
†Transradial arterial approach. §Transfemoral arterial approach.
AMI, acute myocardial infarction; AWMI, anterior wall MI; ECG, electrocardiogram; CK, creatine kinase.

because of the lack of evidence of an additional benefit to AMI patients who underwent primary PCI.30

Stent Implantation
If the lesion size and length could be clearly observed in the IRA following diagnostic coronary angiographic examination, direct stenting was performed during the same procedure. Different stents were used in the present study because of variations in their availability over the time period and included the Crown stent and BX velocity stent (Johnson & Johnson Interventional Systems), NIR, Express and Liberte stents (Boston Scientific), the Wallstent (Schneider, Switzerland), GFX, S760, S-7, and Driver stents (Medtronic AVE), and the Duet, Multilink, Penta, and Vision stents (Guidant Co). No drug-eluting stents were used in the current study.

Indication for IABP Support
IABP support was performed using the right or left TFA in patients with acute pulmonary edema associated with an unstable condition or hemodynamic instability. Other indications for IABP support were angiographic evidence of slow-flow or the no-reflow phenomenon or heavy thrombus formation in the IRA.

Definitions
AMI was defined as typical chest pain lasting >30 min with ST-se >1 mm in 2 consecutive precordial or inferior leads. Procedural success was defined as successful primary stenting at the desired position with a residual stenosis <20% or residual stenosis <30% for balloon angioplasty followed by TIMI grade 3 flow in the IRA. Multivessel disease was defined as stenoses >50% in ≥2 major epicardial coronary arteries. The definition of unsuccessful reperfusion was a final TIMI flow ≤2 in the IRA after primary PCI.

Quantitative angiographic analysis (QCA) of the percent-ages of luminal-diameter stenosis, lesion length, and luminal diameters was performed using a digital edge-detection algorithm (DUQUE System) and selection of end-diastolic frames demonstrating the stenosis in its most severe and non-foreshortened projection. With the contrast-filled guiding catheter as the calibration standard, the reference and luminal diameters were calculated before and after angioplasty.

Major vascular bleeding was defined as bleeding related to the procedure with a fall in hemoglobin >3 g/dl requiring a blood transfusion. A major vascular complication was defined as the formation of a pseudoaneurysm or arteriovenous fistula.

Statistical Analysis
Data are expressed as mean±SD. Continuous data were analyzed using the t-test and categorical data were analyzed using the chi-square test. Statistical analysis was performed using SAS Statistical Software for Windows version 8.2 (SAS institute, Cary, NC, USA). P<0.05 was considered statistically significant.

Results
Baseline Characteristics of the Study Patients (Table 1)
There were no significant differences between the 2 groups in terms of age, gender, incidence of hypertension or hypercholesterolemia, and the incidence of previous stroke was similar between groups. However, the incidence of current smoking was notably higher, and the incidence of diabetes mellitus significantly lower, in Group 2 than in Group 1 and, moreover, the incidence of old MI was notably higher in Group 2.

The incidences of Killip 3 and combined ≤Killip 2 scores did not differ between Group 1 and Group 2 upon presentation, and the electrocardiographic finding of anterior wall MI infarction was similar between the 2 groups. However, the peak CK level was significantly increased in Group 2 compared with Group 1. Furthermore, the incidence of pre-infarct angina and of angiographic collateral circulation in the IRA was notably higher in Group 2 than in Group 1.

Angiographic Findings, Frequency of IABP Support and Stent Implantation (Table 2)
The incidence of multivessel disease and the distribution of IRA did not differ between Groups 1 and 2. On the other hand, although the pre-PCI TIMI flow grades were similar between the 2 groups, the incidence of post-TIMI grade 3 flow was significantly higher in Group 1 than in Group 2. Moreover, despite similar time from puncture to first balloon inflation between the 2 groups, the procedural time was significantly longer in Group 2 than in Group 1.
Angiographic findings demonstrated that the lesion length was notably increased in Group 1 compared with Group 2. The pre-PCI MLD was significantly increased and the pre-PCI RLD significantly decreased in Group 1 compared with Group 2. Furthermore, the post-PCI MLD was notably increased in Group 1, but the post-PCI RLD were similar between the 2 groups. On the other hand, the use of IABP support was significantly lower in Group 1 than in Group 2. Conversely, the incidence of stent implantation and of adjunctive tirofiban therapy was remarkably higher in Group 1 than in Group 2.

Final TIMI grade 3 flow did not differ between stent implantation and balloon angioplasty in Group 1 [94.3% (378/401) vs 87.6% (92/105), P>0.05] or Group 2 patients [87.8% (354/403) vs 89.2% (363/407), P=0.547].

Discussion

The results of the present study, which investigated the safety and efficacy of using the TRA vs the TFA in patients with AMI undergoing primary PCI, have several striking clinical implications. First, to the best of our knowledge, this is the largest series investigating the safety and feasibility of using the TRA for patients with AMI undergoing primary PCI. Second, our study identified that TRA is safe and efficacious for ≤Killip 3 AMI patients undergoing both diagnosis and primary PCI. Third, our study further demonstrated that TRA is not inferior to TFA in terms of the time taken from puncture to first balloon inflation, procedure time, procedural success rate, the duration of hospital stay and 30-day clinical outcome. Finally, a significant reduction in bleeding/vascular complications was noted in patients undergoing the TRA approach compared with their TFA counterparts.

Rationale of TRA for Patients With AMI Undergoing Primary PCI

Brisk TIMI grade 3 flow immediately after thrombolytic therapy or primary PCI in patients with AMI is the desired result to minimize the effect of the ischemic insult on the myocar-
Arteries. Primary PCI using the TRA was performed in simultaneously IABP and ECMO support via both femoral patient required IABP support, including 12 patients with required for patients with AMI complicated by cardiogenic complications in such an AMI setting. TFA would increase the incidence of vascular and bleeding normal blood flow in the IRA.

Frequently required for post-thrombolytic therapy patients ing the GUSTO trial. 3 flow in the IRA, as reported in many clinical trials, includ

Thrombolytic therapy remains the standard therapy for AMI patients, but it can only achieve <55% of TIMI grade 3 flow in the IRA. As expected, PCI via the TFA approach for ≤Killip 3 AMI patients undergoing primary PCI and we strongly recommends the use of the TRA as the preferred alternative for such patients. To the best of our knowledge, Saito et al.40 were the pioneers in comparing the safety and feasibility of the TRA and TFA approaches for patients with AMI undergoing primary PCI. Their results demonstrated that for selective patients with AMI, the TRA is comparable to the TFA in terms of the success rate of reperfusion and the incidence of in-hospital major adverse clinical events. Later, our team also demonstrated the safety of using the TRA with the PercuSurge device for distal protection from embolization in AMI patients undergoing primary PCI, with promising clinical outcome.27 Therefore, the present results support the those from previous studies.26,27

Other Potential Therapeutic Options of Using the TRA in AMI Patients

Thrombolytic therapy remains the standard therapy for AMI patients, but it can only achieve ≤55% of TIMI grade 3 flow in the IRA, as reported in many clinical trials, including the GUSTO trial.39 Therefore, rescue therapy by PCI is frequently required for post-thrombolytic therapy patients with ongoing chest pain caused by failure in achieving normal blood flow in the IRA.40,41 As expected, PCI via the TFA would increase the incidence of vascular and bleeding complications in such an AMI setting.39 Extrapolating the results of the current study, we suggest that the TRA would be a relatively safer option for treating post-thrombolytic AMI patients.

In real-world clinical practice, IABP support is frequently required for patients with AMI complicated by cardiogenic shock. In the current study, >90% of cardiogenic shock patient required IABP support, including 12 patients with simultaneous IABP and ECMO support via both femoral arteries. Primary PCI using the TRA was performed in >50% of cardiogenic shock patients with a detectable radial pulse during our TRA study period, including those 12 patients receiving both IABP and ECMO support. Accordingly, we suggest that the TRA for primary PCI should be considered as the preferred option for cardiogenic shock patients unless the radial pulse cannot be detected. We further suggest that IABP support should initiated first, followed by TRA access.

Study Limitations

There are several issues related to this study, some of which are stent-related. First, different types of stents were used during different time periods because of the evolution in stents, which affected the availability in Taiwan. Second, the incidence of stent placement was higher during the TRA period than during the TFA period because of the limited availability of coronary stenting during the early TFA period. Some would, therefore, argue that stent implantation would improve the final TIMI-3 flow in the IRA, which in turn, would improve the clinical outcome. However, the incidence of post-procedural TIMI grade 3 flow in the IRA did not differ between patients with and without stent implantation. Furthermore, a previous investigation demonstrated that, compared with balloon angioplasty, stent implantation did not offer an additional benefit for patients with AMI complicated by cardiogenic shock undergoing primary PCI.29 Third, the significantly longer procedural time in the TFA group compared with the TRA group could be explained by the increased use of stent implantation in the TRA group, which helped in more effectively achieving optimal angiographic parameters as compared with balloon angioplasty. Fourth, patients with high-burden thrombus formation of the IRA in the TRA study period received distal embolic protection using the PercuSurge device, which has been demonstrated to be effective in improving final TIMI-3 flow. These patients were excluded from the study, which may have contributed to the higher incidence of final TIMI-3 flow in the TRA patient population.16,27

Disclosures

There was no funding in this study and none of the authors has a commercial association, such as consultancies, stock ownership or other equity interests or patent-licensing arrangements.

References

Transradial Arterial Approach for AMI


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