State Study Supports Stand-Alone Primary PCI

BY BRUCE JANCIN

ORLANDO — In patients with ST-elevation MI who were treated with primary percutaneous coronary intervention and enrolled in a large Massachusetts registry study, the 1-year rates of mortality, MI, and target vessel revascularization were similar in hospitals with or without on-site cardiac surgery.

"These data suggest that in no-surgery-on-site hospitals adhering to strict procedural volume requirements and the standards of care outlined in the American College of Cardiology/American Heart Association guidelines, primary PCI for STEMI patients may be performed with no difference in mortality through 1 year," Dr. Ather Anis said.

Primary PCI is recommended in the ACC/AHA guidelines as the reperfusion therapy of choice for STEMI when it can be accomplished in a timely manner. But most STEMI patients present to hospitals that don't perform primary PCI because they lack surgery on-site (SOS). Performing primary PCI in STEMI patients at non-SOS hospitals—provided that it can be done safely—would be a strategy to improve access to the procedure, explained Dr. Anis of Boston University at the annual scientific sessions of the AHA. He reported on 3,018 Massachusetts STEMI patients who had primary PCI during 2005-2007, including 977 treated at non-SOS hospitals through a state department of health pilot program.

One-year mortality and most other key outcomes were similar regardless of hospital type. (See box.) The exceptions were 30-day all-cause mortality, which was significantly lower in STEMI patients who had their primary PCI at non-SOS hospitals, and 30-day and 1-year repeat revascularization rates, which were significantly higher at non-SOS hospitals.

Dr. Spencer B. King III, president of the Saint Joseph's Heart and Vascular Institute and professor of medicine emeritus at Emory University, both in Atlanta, observed, "You can't say a well-run primary PCI program without surgery on-site isn't as good as one with surgery on-site."

However, Dr. Robert A. Guyton, professor of surgery and chief of cardiothoracic surgery at Emory, said that the data "don't really give you comfort" that STEMI patients have the same outcomes whether they present to hospitals with or without SOS, because the registry collected data only on the STEMI subgroup undergoing primary PCI, not on all comers with STEMI.

"We do this all too often in medicine, talking about results in patients in whom we choose to perform an intervention," Dr. Guyton said. " What the patient—and the state of Massachusetts—wants to know is, 'What is my outcome if I am taken with my STEMI to a hospital without surgery on-site versus my outcome if I am taken to a hospital with SOS?' "

Although the Massachusetts registry study does not address that question, a new report from the National Registry of Myocardial Infarction does, he said. The NRMI study included 58,821 STEMI patients who presented to PCI-capable hospitals during 2004-2006. The 8.1% of patients presenting to non-SOS hospitals had 9.8% mortality, significantly higher than the 7.0% mortality in patients presenting to SOS hospitals. The patients at non-SOS hospitals also had a significantly lower rate of reperfusion (71% vs. 81%), less use of guideline-recommended medications, and a trend for less use of primary PCI (44% versus 56%). "If I'm in the ambulance with a STEMI, I'm going to request to be taken to an SOS hospital," Dr. Guyton concluded.

In an interview, Dr. Elliott M. Antman pointed out that ACC/AHA guidelines already support primary PCI for STEMI at non-SOS hospitals as a class IIb recommendation. "What would it take to actually move the needle from class IIb to a class I recommendation? Our rules of evidence would require a randomized trial," said Dr. Antman, a member of the ACC/AHA guidelines-writing committee and professor of medicine at Harvard Medical School, Boston.

Dr. Anis reported no financial conflicts. ■

Primary PCI Outcomes in Hospitals With or Without Cardiac Surgery On-Site

End Point	SOS hospitals	non-SOS hospitals
*30-day all-cause mortality	5.7%	4.5%
1-year mortality	9.4%	8.6%
30-day MI	2.8%	4.4%
1-year MI	5.1%	6.7%
*30-day repeat revascularization	7.6%	14.9%
*1-year repeat revascularization	14.7%	21.0%
30-day target vessel revascularization	6.3%	5.0%
1-year target vessel revascularization	10.9%	9.7%

*Statistically significant difference between SOS and non-SOS hospitals.

Note: Based on data from 2,041 patients treated at SOS hospitals and 977 treated at non-SOS hospitals.

Source: Dr. Anis

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All-Cause Mortality Dropped

Ticagrelor *from page 1*

a significant 15% relative risk reduction.

Ticagrelor was also associated with significant advantages over clopidogrel in key secondary end points in PLATO STEMI, including reductions of 18% in all-cause mortality and 39% in definite stent thrombosis. (See box.) Moreover, there was no increase in major bleeding with ticagrelor, reported Dr. Steg, professor of cardiology at the University of Paris and director of the coronary care unit at Bichat-Claude Bernard Hospital.

Ticagrelor is a reversible blocker of the P2Y12 platelet receptor with considerably more potent and consistent antiplatelet activity than clopidogrel. It's the first in a new class of agents known as the cyclo-pentyl-triazolo-pyrimidines that is chemically distinct from thienopyridines such as clopidogrel or prasugrel.

In PLATO STEMI, the number of patients who needed to be treated for 1 year with ticagrelor rather than clopidogrel to prevent one additional cardiovascular death, MI, or stroke was 59, Dr. Steg said.

He drew particular attention to the reduction in all-cause mortality with ticagrelor compared with clopidogrel, an advantage that grew over time. "We don't come across treatments in cardiovascular care that reduce all-cause mortality often. It sets ticagrelor apart from other oral inhibitors of platelet function. The mortality reduction here is new, it is important quantitatively, and it may have several explanations," the cardiologist said.

For one thing, ticagrelor is probably not solely a platelet inhibitor. It is also an adenosine agonist.

"Adenosine has myriad physiologic functions that may be beneficial in the context of acute myocardial ischemia and vascular disease. It improves platelet function and vascular function and may have myocardial protection properties. This is very speculative, but given that other antiplatelet agents that have reduced MI have not decreased mortality, the fact that we see here a decrease in MI and cardiovascular events, and a decrease in mortality, raises the question of whether there are other mechanisms at play," he said.

Discussant Lisa K. Jennings, Ph.D., a vascular biologist at the University of Tennessee, Memphis, noted that another possible contributor to ticagrelor's all-cause mortality advantage may be its faster onset of action. Unlike the thienopyridines, ticagrelor is not a prodrug. And PLATO STEMI participants were randomized relatively early—within the first 24 hours after symptom onset, when their risk of cardiac events was especially high and a mortality difference favoring a faster-acting drug would be particularly evident.

The chief side effect associated with ticagrelor was dyspnea, occurring in 12.9% of patients, compared with 8.3% of patients on clopidogrel. The dyspnea was mild, usually occurred early in the course of treatment, and then resolved. Only 0.5% of patients assigned to ticagrelor discontinued the study drug because of dyspnea.

Reassuringly, the rate of bradycardia-related events, including syncope and heart block, was not any greater with ticagrelor than with clopidogrel.

The reduction in cardiovascular events seen with ticagrelor could be expected to result in considerable financial savings through reduced post-STEMI hospitalizations.

In addition, the drug's stronger and more consistent antiplatelet activity compared with clopidogrel could conceivably do away with the need to perform platelet function assays in patients undergoing PCI, as is now guideline-recommended with clopidogrel. That possibility will require further studies.

The main results of the PLATO study, involving close to 19,000 patients with acute coronary syndrome, were presented earlier in the year at the annual meeting of the European Society of Cardiology.

AstraZeneca, which sponsored PLATO, recently applied for European marketing approval for ticagrelor (Brilinta) for treatment of patients with acute coronary syndrome. The company plans to file with the Food and Drug Administration before the end of the year. ■

PLATO STEMI: Key 1-Year Outcomes

	Clopidogrel	Ticagrelor	Relative Risk Reduction
All-cause mortality	6.0%	4.9%	18%
Definite stent thrombosis	2.5%	1.6%	39%
Major bleeding	9.3%	9.0%	Nonsignificant

Source: Dr. Steg

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VITALS

Major Findings: STEMI patients treated with aspirin plus ticagrelor had significantly fewer major cardiovascular events at 1 year than did patients treated with aspirin plus clopidogrel, with no increase in major bleeds.

Source of Data: 8,430 patients in the prespecified STEMI subanalysis of the PLATO trial.

Disclosures: Dr. Steg is a consultant to, and on the speakers bureau for, AstraZeneca. Dr. Jennings is also a consultant to the company.