CORRESPONDENCE

Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting

TO THE EDITOR: With regard to the results of the SYNTAX (Synergy between PCI [percutaneous coronary intervention] with Taxus and Cardiac Surgery) study (ClinicalTrials.gov number, NCT00114972) reported by Serruys et al. (March 5 issue),[1] we wish to highlight a few factors that require clarification and may influence the differences observed between the study groups. The timing of strokes and rates of atrial fibrillation are not reported. These data, in combination with the differences in pharmacologic therapies between cohorts, may account for the excess number of strokes seen in the coronary-artery bypass grafting (CABG) cohort. Clarification of the timing of strokes may help to explain whether they were thromboembolic or due to surgical handling of the aorta. Furthermore, the range and influence of PCI strategies, including the use of adjuvant intravascular ultrasonography adopted by the investigators for complex lesions, are not reported; these factors could have affected restenosis rates.

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1. Serruys PW, Morice M-C, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360:961-72.

TO THE EDITOR: In the SYNTAX trial, the rate of stroke was significantly higher in the CABG group than in the PCI group (2.2% vs. 0.6%). The authors speculate that a lower rate of thienopyridine use in the CABG group contributed to this finding. However, although the benefit of dual-antiplatelet therapy after PCI[1] or acute coronary syndrome[2] is well established, the number of patients in the CABG group with evidence-based indications for dual-antiplatelet therapy is not reported. Furthermore, the major trials comparing prolonged dual-antiplatelet therapy with aspirin alone have shown only modest reductions in stroke, with relative risk reductions ranging from 10% to 21%.[1-3] Thus, differential rates of thienopyridine use played at most a minor role in the SYNTAX findings. Data on the timing of strokes with respect to the intervention may shed light on the extent to which stroke is an unavoidable risk of CABG versus a consequence of differential postintervention medical treatment.

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aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;345:494-502. [Errata, N Engl J Med 2001;345:1506, 1716.]
3. Bhatt DL, Fox KAA, Hacke W, et al. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med 2006;354:1706-17.

TO THE EDITOR: It is regrettable that the organizers of the SYNTAX trial chose to compare a percutaneous stenting procedure with a standard CABG operation known to confer a risk of stroke of 1 to 2%.

Evidence is accumulating[1-3] that the prevalence of procedure-related stroke is significantly diminished when "anaortic" techniques (i.e., surgery conducted without cardiopulmonary bypass and without aortic manipulation) are used. Three reports each describe more than 1000 such CABG operations, and with all these operations the rate of stroke was less than 0.3%.

To our knowledge, no randomized trial has compared standard with anaortic coronary surgery; however, in our experience, it is a safe procedure in almost all patients with triple-vessel disease or stenosis of the left main coronary artery.

The statement that the incidence of stroke is higher with surgery than with stenting[4] may be true for some operations, but it is not true for others. The incidence of stroke at Royal North Shore Hospital, Sydney, from 2002 through 2006 and the incidence of stroke at two other institutions are shown in Table 1.

Table 1. Rate of Stroke Associated with Anaortic CABG as Compared with Conventional On-Pump and Off-Pump CABG.*

Reference and CABG Procedure	Patients	Strokes
	no.	%
Vallely et al.[1]		
Anaortic	1201	0.25
Off-pump side clamp†	557	1.08
On-pump	1599	1.81
Calafiore et al.[2]		
Anaortic	1533	0.19
Off-pump side clamp†	460	1.09
On-pump	2830	1.44
Prapas et al.[3]		
Anaortic	1359	0.22

* CABG denotes coronary-artery bypass grafting.
† Off-pump side clamp is surgery conducted without cardiopulmonary bypass but with proximal graft anastomoses sutured to the aorta with the use of a conventional side-occlusion clamp.

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1. Vallely MP, Potger K, McMillan D, et al. Anaortic techniques reduce neurological morbidity after off-pump coronary artery bypass surgery. Heart Lung Circ 2008;17:299-304.
2. Calafiore AM, Di Mauro M, Teodori G, et al. Impact of aortic manipulation on incidence of cerebrovascular accidents after surgical myocardial revascularization. Ann Thorac Surg 2002;73:1387-93.
3. Prapas SN, Panagiotopoulos IA, Hamed Abdelsalam A, et al. Predictors of prolonged mechanical ventilation following aorta no-touch off-pump coronary artery bypass surgery. Eur J Cardiothorac Surg 2007;32:488-92.
4. Lee TH, Hillis LD, Nabel EG. CABG vs. stenting — clinical implications of the SYNTAX trial. N Engl J Med 2009;360:e10 (Web only). (Available at http://NEJM.org.)

TO THE EDITOR: The study results reported by the SYNTAX investigators show that at 12 months, the rate of stroke was significantly higher in the CABG group than in the PCI group (2.2% vs. 0.6%, P=0.003). At baseline, the proportion of patients with a history of stroke was 3.9% in the PCI group and was slightly higher (4.8%) in the CABG group (P=0.33). Abundant data provide support for the use of statins in patients undergoing CABG unless statin therapy is contraindicated.[1] Multiple meta-analyses have shown the usefulness of statin therapy for primary and secondary prevention of stroke because of its lipid-lowering and pleiotropic effects.[2,3] Therefore, it is surprising to see that in the SYNTAX trial, only 74.5% of patients in the CABG group received statin therapy, whereas in the PCI group, 86.7% of patients received statin therapy (P<0.001). We believe it is important to know the incidence of stroke and also the contraindications to statin therapy, if any, in the subgroup in which subjects did not receive statin therapy after CABG as compared with other subgroups.

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1. Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). Circulation 2004;110:1168-76. [Erratum, Circulation 2005;111:2014.]
2. Goldstein LB. Statins for stroke prevention. Curr Atheroscler Rep 2007;9:305-11.
3. Rodríguez-Yáñez M, Agulla J, Rodríguez-González R, Sobrino T, Castillo J. Statins and stroke. Ther Adv Cardiovasc Dis 2008;2:157-66.

TO THE EDITOR: Serruys et al. compared the 1-year outcomes of PCI with those of CABG in patients with multivessel disease. The reported superiority of CABG was based solely on a lower rate of repeat revascularization in the CABG group. However, no information is provided on the criteria leading to repeat coronary angiography. Was documentation of ischemia required? This information is critical, since it is known that the threshold for coronary angiography and for coronary revascularization in clinical practice is lower after PCI than after CABG.[1] Indeed, repeat surgery or PCI of a native vessel in patients who previously underwent CABG is associated with an increased procedural risk and worse outcomes.[2-4] Therefore, we would like to know whether the proportion of patients with any signs or symptoms of ischemia at follow-up who underwent angiographic assessment and the proportion of such patients who subsequently underwent revascularization were similar in the two groups. In our view, the lower threshold bias for coronary angiography and for repeat revascularization in the PCI group may have significantly influenced the overall study results.

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1. Loponen P, Korpilahti K, Luther M, Huhtala H, Tarkka MR. Repeat intervention after invasive treatment of coronary arteries. Eur J Cardiothorac Surg 2009;35:43-7.
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THE AUTHORS REPLY: Bhindi and Figtree ask whether the timing of strokes or rates of atrial fibrillation might explain the excess strokes in the CABG group. Similarly, Edwards comments that data on the timing of strokes relative to the intervention may shed light on this difference. Of the 19 strokes that occurred in the CABG group, more than 40% were periprocedural or occurred within 5 days after the procedure. Three of the strokes occurred before the index procedure and were not related to the surgery but were included in the count, reflecting the intention-to-treat analysis. Rates of atrial fibrillation were low among the patients in the CABG group who had a stroke. Given these numbers, neither preprocedural stroke nor atrial fibrillation contributed to the increased rate of stroke in the CABG group. Bhindi and Figtree also discuss the potential influence of the use of adjuvant intravascular ultrasonography on restenosis rates. In the PCI group, 113 patients (12.5%) underwent intravascular ultrasonography.

Brereton et al. are correct in stating that not all surgical techniques are associated with the same risk of stroke; however, we tested the current, standard techniques used in Europe and the United States. Off-pump CABG was performed in 15% of patients in the CABG group; this rate is similar to the rates observed in the United Kingdom and the United States (approximately 20%).[1,2] Data on whether a surgical procedure was a "no-touch" CABG, avoiding manipulations of the aorta, were not captured in the SYNTAX trial.

Shil et al. express concern regarding statin use in patients treated with CABG. Of the patients who had a stroke, 58% of patients in the CABG group and 50% of patients in the PCI group received statins; these rates were lower than those in the overall patient groups (at 12 months, 82% of patients in the CABG group and 86% of patients in the PCI group received statins). Data on the contraindications for statin use were not collected.

In response to the comments of Bonvini et al.: angiographic assessment was not required by the protocol within the first 12 months. Therefore, any angiographic assessment was performed at the physicians' discretion. Some study sites followed their institutional guidelines, which at the time of the study called for routine follow-up angiograms, particularly in patients with lesions in the left main coronary artery. In total, 207

angiograms were obtained within 12 months (in 56 patients in the CABG group and in 151 patients in the PCI group). The primary indications leading to angiography were angina in 29 patients in the CABG group (14.0%) and 95 patients in the PCI group (45.9%), myocardial infarction in 10 patients in the CABG group (4.8%) and 19 patients in the PCI group (9.2%), an abnormal stress test in 5 patients in the CABG group (2.4%) and 2 patients in the PCI group (1.0%), and myocardial ischemia in 1 patient in the CABG group (0.5%) and 12 patients in the PCI group (5.8%).

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2. Society of Thoracic Surgeons National Adult Cardiac Database: spring report 2007. Durham, NC: Duke Clinical Research Institute, June 2007.

Melamine-Contaminated Powdered Formula and Urolithiasis

TO THE EDITOR: The article by Guan et al.,[1] the accompanying editorial by Langman,[2] and the letter to the Editor by Wang et al.[3] (all in the March 12 issue) provide information about the epidemiology of pediatric nephrolithiasis caused by melamine poisoning. Here we supplement those data and commentary with information regarding diagnosis and treatment on the basis of our clinical experience and the advice of the Chinese Ministry of Health.[4,5]

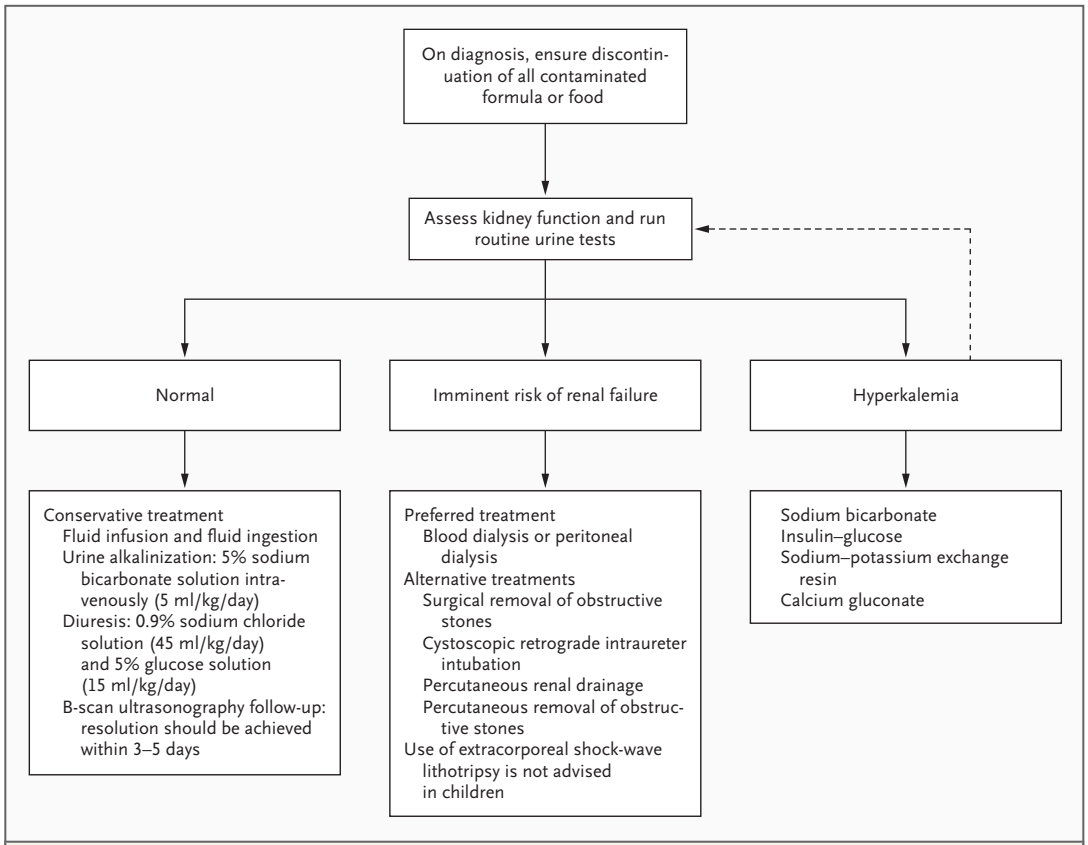

Figure 1. Treatments for Pediatric Nephrolithiasis Caused by Melamine Poisoning as Recommended by the Chinese Ministry of Health.