Role of Renin-Angiotensin System Inhibitors in Patients Undergoing Off-Pump Coronary Artery Bypass Grafting

Takeshi Kinoshita, MD; Tohru Asai, MD, PhD

Renin-angiotensin system (RAS) inhibitors have potential benefit for patients undergoing coronary artery bypass grafting (CABG).\(^1\)\(^–\)\(^4\) In the Effects of Quinapril on Vascular Angiotensin-Converting Enzyme and Determinants of Ischemia trial, patients were randomized 4 weeks before CABG to receive either quinapril (40 mg/day) or placebo for 1 year after surgery.\(^1\) Patients treated with quinapril had a 77% reduction in ischemic events (death, revascularization, myocardial infarction, recurrence of angina pectoris, ischemic stroke, or transient ischemic attack stroke; 15% vs 4%; P=0.04). Quinapril was well tolerated and was not associated with any untoward perioperative hemodynamic events. In a propensity-score-based analysis of 481 patients undergoing isolated on-pump CABG,\(^5\) the postoperative cardiac troponin I peak concentration was lower in patients receiving preoperative angiotensin-converting enzyme (ACE) inhibitors (1.6 ng/ml (1.05–3.40) vs 2.4 ng/ml (1.13–6.10); P=0.0006). Preoperative ACE inhibitors were found to decrease the postoperative cardiac troponin I peak concentration (P=0.004) and to lower the rates of postoperative myocardial infarction (2.0% vs 4.2%; P=0.25) and low cardiac output syndrome (3.6% vs 6.3%; P=0.24).

The association between preoperative treatment with RAS inhibitors and postoperative acute kidney injury (AKI) has been investigated in patients undergoing on-pump cardiac surgery, with conflicting results.\(^5\)\(^–\)\(^7\) Benedetto et al evaluated the effect of preoperative ACE inhibitors on the occurrence of postoperative AKI in a propensity-score-based analysis of 536 patients undergoing on-pump CABG.\(^5\) The incidence of AKI was 6.4% in patients who received preoperative ACE inhibitors and 12.2% in patients who did not (P=0.02). The incidence of AKI requiring dialysis was 2.4% in the treatment group and 6.3% in controls (P=0.03). After adjusting for propensity score and covariates, administration of preoperative ACE inhibitors was found to reduce the incidence of postoperative AKI (odds ratio, 0.48; 95% confidence interval (CI), 0.23–0.77; P=0.04). In a retrospective analysis of 346 patients who were ≥65 years old and underwent elective cardiac surgery,\(^6\) preoperative RAS inhibitors significantly and independently reduced the incidence of postoperative AKI compared with those not taking them: 1.6% vs 7.6%, yielding an odds ratio of 0.19 (95%CI, 0.04–0.84, P=0.029). Those authors concluded that preoperative RAS inhibitors may have significant renoprotective effects for aging patients undergoing elective cardiac surgery. On the other hand, Arora et al retrospectively analyzed a cohort of 1,358 patients undergoing on-pump cardiac surgery and demonstrated that preoperative use of RAS inhibitor increased the risk for postoperative AKI by 27.6%.\(^7\)

The off-pump technique is reportedly associated with a reduced incidence of AKI,\(^8\)\(^–\)\(^11\) but to date there has not been a study that investigated the effect of preoperative use of RAS inhibitors on AKI after off-pump CABG (OPCABG).

In this issue of the Journal, Yoo et al evaluated the effects of RAS inhibitors on postoperative renal function in patients undergoing isolated OPCABG.\(^8\) The incidence of postoperative AKI was similar between patients treated with RAS inhibitors and those not treated (19.9% vs 20.9%, P=0.815). The highest postoperative serum creatinine levels were similar between the groups (1.2±0.4 mg/dl vs 1.2±0.5 mg/dl, P=0.078). In a multivariate logistic regression using propensity scores, preoperative treatment with RAS inhibitors was not a risk factor of postoperative AKI (odds ratio, 0.841; 95%CI, 0.503–1.407; P=0.509). Diabetes, preoperative creatinine levels, and perioperative transfusion were independently associated with postoperative AKI. The authors concluded that off-pump could be a safe alternative to on-pump CABG without additionally increasing the risk of developing AKI in patients who would benefit from continued RAS inhibitor therapy.\(^4\)

This new evidence will encourage cardiac surgeons to use RAS inhibitors in OPCABG patients, but the other remarkable point is that mean arterial pressure was lower and the amount of norepinephrine infusion during operation was larger in patients who received RAS inhibitors than in those did not. Hypotension during positioning of the heart is a matter of concern during OPCABG. Emergency conversion to cardiopulmonary bypass because of hemodynamic compromise is reported to be associated with higher rates of mortality and morbidity.\(^9\)

We need to recognize an important limitation to this study (ie, the inclusion of only “successfully treated” patients), otherwise the conclusion can lead to misunderstanding. The authors preliminarily excluded the following patients from the analysis: those who failed to take RAS inhibitors for 2 weeks before surgery, because of deterioration in renal function or hypotension, and those who required urgent conversion to cardiopulmonary bypass because of hemodynamic instability. Also we need to know whether or not hypoten-

The opinions expressed in this article are not necessarily those of the editors or of the Japanese Circulation Society.

Received July 16, 2010; accepted July 16, 2010; released online August 10, 2010

Department of Surgery, Shiga University of Medical Science, Otsu, Japan

Mailing address: Tohru Asai, MD, PhD, Department of Surgery, Shiga University of Medical Science, Otsu Tsukinowacho, Otsu 520-2192, Japan. E-mail: toru.asai@belle.shiga-med.ac.jp


All rights are reserved to the Japanese Circulation Society. For permissions, please e-mail: cj@j-circ.or.jp
sion, possibly caused by RAS inhibitors, affected the conversion rate, the revascularization rate or operative mortality and morbidity.

There is growing evidence that RAS inhibitors should be used in patients undergoing CABG. In OPCABG patients, RAS inhibitors do not have a negative effect on postoperative renal function. However, intraoperative hypotension is a potential side-effect of preoperative use of RAS inhibitors.

References


