Ismail Yurekli, MD

Mert Kestelli, MD

Habib Cakir, MD

Department of Cardiovascular

Surgery

Izmir Ataturk Education and Research

Hospital

Izmir, Turkey

References

1. Michler RE, Rouleau JL, Al-Khalidi HR, Bonow RO, Pellikka PA, Pohost GM, et al; STICH Trial Investigators. Insights from the STICH trial: Change in left ventricular size after coronary artery bypass grafting with and without surgical ventricular reconstruction. *J Thorac Cardiovasc Surg*. October 27, 2012 [Epub ahead of print].
2. Athanasuleas CL, Buckberg GD. Surgery for the failing heart after myocardial infarction. *Anadolu Kardiyol Derg*. 2008;8(Suppl 2):93-100.

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WHICH IS MORE IMPORTANT IN THE POTENTIAL INTERFERENCE ON CARDIOPROTECTION BY REMOTE ISCHEMIC PRECONDITIONING: β -BLOCKERS OR ANESTHETIC CHOICE?

To the Editor:

We read with great interest the paper from Kottenberg and colleagues,¹

FIGURE 1. Metaregression plot of β -blockers (%) on standardized mean difference (SMD) of myocardial biomarkers in coronary artery bypass grafting (coefficient of 0.0258, $P = .092$). Original data from Zhou and associates.⁴

recently published online in the *Journal*. Building on their previous study,² they have conducted 2 impressive independent works to explore the cardioprotection by remote ischemic preconditioning (RIPC) with isoflurane³ or propofol¹ in coronary artery bypass grafting (CABG).¹⁻³

There has always been concern regarding whether β -blockers could interfere with the cardioprotective effect of RIPC. In their fundamental study,² the mean β -blocker usage rates were 60% in the propofol substudy and 64% in the isoflurane substudy,

and a better preservation of RIPC-induced cardioprotection with isoflurane than propofol was proposed. This difference seems to remain unchanged in the population, however, with higher proportion of β -blocker medication (83% in propofol¹ group and 87% in isoflurane).³ Their series of studies indicates that the anesthetic choice is more critical than β -blocker use in the interference of cardioprotection by RIPC.

Nevertheless, our group's recent meta-analysis,⁴ which included 15 randomized, controlled trials with

TABLE 1. Results in metaregression and subgroup analyses

Variables		Coefficient or SMD			Adjusted R^2 or $P_{\text{Difference}}$ value
Univariate analysis	No. of comparisons	Coefficient	95% CI	P value	Adjusted R^2
β -blockers (%) (CABG only)	11	0.0258	-0.0052 to 0.0567	.092	0.22
β -blockers (%)	14	0.0161	0.0028-0.0295	.022	0.37
Volatile agents	16	0.6617	-0.0481 to 1.3716	.065	0.23
Multivariate analysis		Coefficient			Adjusted R^2
β -blockers (%)	14	0.0129	-0.00234 to 0.0282	.089	0.38
Volatile agents	14	0.4037	-0.5019 to 1.3092	.348	
Subgroup analysis		SMD			$P_{\text{Difference}}$ value
β -blockers (%)	14	-0.28	-0.61 to -0.04	.09	.02
>75%	5	0.18	-0.26 to 0.61	.43	
$\leq 75\%$	9	-0.56	-0.96 to -0.16	.006	
Volatile agents	15	-0.28	-0.57 to -0.02	.06	.01
Volatile	12	-0.11	-0.41 to 0.19	.46	
Nonvolatile	4	-0.81	-1.28 to -0.34	.0008	

Original data from Zhou and associates.⁴ SMD, Standardized mean difference; CI, confidence interval; CABG, coronary artery bypass grafting.

1155 adult patients undergoing cardiac surgery, found that both β -blockers and volatile anesthetics are potentially influential factors in cardioprotection by RIPC, a finding confirmed in univariate metaregression and subgroup analyses. The role of β -blockers remained significant in the CABG subgroup (Figure 1). In addition, the potential interference of β -blockers was independent of volatile anesthetics in the subsequent multivariate analysis (Table 1). Moreover, previous studies that used animal hearts or human isolated atrial trabeculae have suggested that β -blockers could abolish the cardioprotection of ischemic or anesthetic preconditioning (see discussion in reference 4). In addition, no cardiac benefit from RIPC in CABG was observed in Lucchinetti and associates' study,⁵ which had a mean β -blocker proportion of 91%. These evidence suggested greater significance of β -blockers in the cardioprotective effect of RIPC, which is thus more important in the potential interference with cardioprotection by RIPC.

Is it β -blockers or anesthetic choice? The findings from my group are based mainly on the aggregate patient data. We are therefore interested to know whether this would hold true for the individual patient data in Kottenberg and colleagues' study² if multivariate linear regression analyses at least including β -blockers and anesthetic choice in a total of 72 patients were performed.

Yang Liu, MD^a

Li Ma, MD^b

^aDepartment of Intensive Care Unit

^bCellular & Molecular Biology

Beijing Chest Hospital

Capital Medical University

Beijing, China

References

1. Kottenberg E, Musiolik J, Thielmann M, Jakob H, Peters J, Heusch G. Interference of propofol with signal transducer and activator of transcription 5 activation and cardioprotection by remote ischemic

preconditioning during coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. March 1, 2013 [Epub ahead of print].

2. Kottenberg E, Thielmann M, Bergmann L, Heine T, Jakob H, Heusch G, et al. Protection by remote ischemic preconditioning during coronary artery bypass graft surgery with isoflurane but not propofol—a clinical trial. *Acta Anaesthesiol Scand*. 2012;56:30-8.
3. Heusch G, Musiolik J, Kottenberg E, Peters J, Jakob H, Thielmann M. STAT5 activation and cardioprotection by remote ischemic preconditioning in humans: short communication. *Circ Res*. 2012; 110:111-5.
4. Zhou C, Liu Y, Yao Y, Zhou S, Fang N, Wang W, et al. β -blockers and volatile anesthetics may attenuate cardioprotection by remote preconditioning in adult cardiac surgery: a meta-analysis of 15 randomized trials. *J Cardiothorac Vasc Anesth*. 2013;27:305-11.
5. Lucchinetti E, Bestmann L, Feng J, Freidank H, Clanchan AS, Finegan BA, et al. Remote ischemic preconditioning applied during isoflurane inhalation provides no benefit to the myocardium of patients undergoing on-pump coronary artery bypass graft surgery: lack of synergy or evidence of antagonism in cardioprotection? *Anesthesiology*. 2012;116:296-310.

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DEFINITION OF LOCAL AND REGIONAL RECURRENCE IN THE AMERICAN COLLEGE OF SURGERY ONCOLOGY GROUP Z0030 TRIAL

To the Editor:

We read with great interest the report by Darling and colleagues¹ regarding the impact on patient survival of mediastinal lymph node dissection (MLND) during lung cancer surgery. This study focused strictly on whether MLND had any impact on survival relative to reliable mediastinal lymph node sampling. This is one of the most challenging questions in thoracic surgery; to answer it, Darling and colleagues¹ prepared and executed an elaborate protocol. Although the result was negative—that is, MLND did not show any survival benefit relative to mediastinal lymph node sampling—the data acquired from this study are of great clinical value for benchmarking. Whereas this study was carried out by authorized expert thoracic surgeons, our *real-world* practice can be assessed by comparing our results with the published outcomes of morbidity and mortality.²

Darling and colleagues¹ reported 285 recurrences, including 54 local,

74 regional, and 225 distant recurrences, in the eligible subject population. Although it is unclear whether each recurrence number was counted by case or site, we are very interested in the definition of the terms, namely, local, regional, and distant recurrence. Because the local and regional recurrence rates vary according to the definition of the terms³ and a standard definition does not currently exist, we would like investigators to specify their definitions of these terms. Several locations should be considered as the recurrence sites in the definition, including bronchial stump, ipsilateral hilum, interlobar staple line, ipsilateral mediastinal lymph node, ipsilateral lung parenchyma, ipsilateral thoracic cavity (pleural dissemination and malignant pleural effusion), contralateral mediastinal/hilum lymph node, supraclavicular lymph node, contralateral lung parenchyma, chest wall, and malignant pericardial effusion. We hope that standard definitions for recurrence sites will be established in the near future.

The American College of Surgery Oncology Group Z0030 trial results continue to produce new findings.⁴ We believe the full utilization of this landmark database is important to improve clinical practice and future studies.

Hideo Ichimura, MD

Yuichiro Ozawa, MD

Department of General Thoracic

Surgery

Tsukuba Medical Center Hospital

Tsukuba, Japan

References

1. Darling GE, Allen MS, Decker PA, Ballman K, Malthaner RA, Inculet RI, et al. Randomized trial of mediastinal lymph node sampling versus complete lymphadenectomy during pulmonary resection in the patient with N0 or N1 (less than hilar) non-small cell carcinoma: results of the American College of Surgery Oncology Group Z0030 Trial. *J Thorac Cardiovasc Surg*. 2011;141:662-70.
2. Allen MS, Darling GE, Pechet TT, Mitchell JD, Herndon JE II, Landreneau RJ, et al. Morbidity and mortality of major pulmonary resections in patients with early-stage lung cancer: initial results of the randomized, prospective ACOSOG Z0030 trial. *Ann Thorac Surg*. 2006;81:1013-9; discussion 1019-20.