the two low-quality trials [2, 3] (RR, 2.22; 95% CI, 0.51 to 9.59; $p = 0.29$; significant heterogeneity [$p = 0.02$]) and the three high-quality trials [4–6] (RR, 1.59; 95% CI, 0.99 to 2.57; $p = 0.06$; no heterogeneity [$p = 0.85$]) demonstrated that OPCAB had no impact on risk of graft occlusion. On the other hand, pooled analysis of all five trials [2–6] demonstrated a statistically significant 56% increase in risk of graft occlusion with OPCAB relative to CABG (RR, 1.56; 95% CI, 1.04 to 2.35; $p = 0.03$; no heterogeneity [$p = 0.14$]). To assess the impact of qualitative heterogeneity in trial design and patient selection on the pooled effect estimate, we performed several sensitivity analyses by excluding individual trials one at a time and re-calculating the pooled RR estimates for the remaining trials. Exclusion of either the trial by Khan and colleagues [2], the trial by Widimsky and colleagues [3], or the trial by Nathoe and colleagues [5] from the analysis of all five trials did not substantively alter the overall result. However, exclusion of either the trial by Lingaas and colleagues [4] or the trial by Puskas and colleagues [6] demonstrated that OPCAB had no impact on risk of graft occlusion.

In the meta-analysis using OR by Parolari and colleagues [1], a statistically significant increased risk of graft occlusion in the OPCAB group was demonstrated, both when all trials were analyzed together and when low-quality and high quality trials were analyzed separately. Nevertheless, in our re-analysis using RR more appropriate than OR, the statistically significant increased risk vanished when low-quality and high-quality trials were analyzed separately, and in two of five sensitivity analyses.

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Reply

To the Editor:

We thank Takagi and colleagues [1] for their interest in our article. However, their criticism concerning the appropriate use of odds ratio (instead of relative risk) is minor, as the use of odds ratio as a measure of relative effect is a totally acceptable method for describing a treatment effect [2].

Also their concerns about robustness of our analysis can be easily ruled out. First, our strategy to address the potential heterogeneity coming from one of the included studies [3], which was one of the two articles included in "Low quality studies," was to repeat the analysis by excluding this study (a clear outlier at funnel plot), as recommended by Cochrane world-accepted guidelines [2]. In addition, it is obvious that in this case, as at this point only one study remained in the "Low quality studies" subsection, there was no more rationale for performing separate analyses between low-quality and high-quality studies. And only the pooled analysis of all the studies, which in our opinion is by far the most informative one, had sense in this case.

Second, also after the exclusion of the "outlier" article [3], the analysis of the data, both with random-effect and fixed-effect models, provided a statistically significant difference in patency rates between on-pump and off-pump coronary bypass surgery, as we stated and published in our article [4].

Third, even after the exclusion of this article [3], all the remaining 4 studies were exceptionally homogeneous in the effect estimation as previously reported [4].

Fourth, since the submission and publication of our article another prospective randomized study reporting patency data in on-pump and off-pump coronary surgery has been published in the literature [5]. Also the pooled analysis of the articles selected in our previous study plus this recently published article confirms the increased risk of graft failure in patients undergoing off-pump coronary surgery (odds ratio = 1.56; 95% confidence interval = 1.20–2.02; $p = 0.0008$) [6].

Unfortunately the problem of reduced conduit patency in off-pump coronary bypass surgery is here to stay.

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Light and Ice Cream

To the Editor:

The Annals of Thoracic Surgery published the results of an experimental study [1] that demonstrated evidence of denervation after transmyocardial revascularization (TMR) with a holmium:yttrium–aluminum–garnet laser and an ultrasonic device. As this work was done in the normal canine myocardium, its applicability to the clinical scenario is questionable, but of greater concern is the incorrect interpretation afforded by the concomitant invited commentary [2].

In this opinion the authors lump together laser revascularization by three different wavelengths of light, cryoablation, radiofrequency, and mechanical methods as the same. This oversimplified view is analogous to stating that the different methods of TMR are akin to different flavors of ice cream. This ignores the well-established fact that with lasers alone, each wavelength of light incites a different tissue reaction and therefore may work by different mechanisms. Furthermore, to give credence to denervation as the key mechanism of laser TMR ignores the thallium, sestamibi, positron-emission tomography, magnetic resonance imaging, echocardiography, and exercise tolerance test data from over 2,000 patients that demonstrate improvement after TMR that can not be attributed to the nervous system [3]. They cite the absence of angina in diabetic patients as similar to TMR patients, but diabetics continue to have infarctions and worsening function, whereas the opposite is seen after TMR treatment. In addition, they surmise that catheter-based percutaneous laser revascularization failed because it could not reach the nerves. More likely it was because the device created less than half the number of the reported surgical TMR channels to a depth of less than one sixth the thickness of the myocardium.

Nihilistic commentaries on revascularization are not new and if we heeded them we would not be using internal mammary arteries except for Vineberg procedures.

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Reply

To the Editor:

We thank Dr Horvath [1] for his interest in our work [2]. His comments allow us to address some apparent misunderstandings that seem to persist in the field of transmyocardial laser revascularization (TMLR).

First, experimental and clinical evidence shows that excimer, holmium:yttrium–aluminum–garnet, and CO_2 lasers, with widely varying wavelengths from 0.308 to 10.6 micrometers, can create transmyocardial channels with a comparable zone of thermal damage, as well as anginal relief in selected patients. Comparable myocardial damage can also be created by radiofrequency systems, for example, implying that it is likely that also non-laser systems may relieve complaints in selected patients with refractory angina. In "Light and Ice Cream" this view is qualified as incorrect, oversimplified, and nihilistic [1]. However, at our institution, a team of physicists, biologists, and physicians studied laser-tissue interactions for 2 decades, resulting in a reference book on optical-thermal response of laser-irradiated tissue and numerous peer-reviewed publications, including one that addresses laser-tissue interactions in TMLR [3, 4]. On that basis we cannot support the statement by Horvath [1] that the previously mentioned lasers when used in TMLR incite a different tissue reaction and work by different mechanisms.

Second, the mechanism of TMLR is still being debated. Unfortunately, irrespective of the system used, to date there is hardly any clinical evidence that TMLR does result in improved perfusion, which is obviously the optimal treatment of angina. Horvath [1] states that in more than 2,000 patients the demonstrated improvement in response to TMLR can not be attributed to denervation, even though this was investigated in only 8 of these patients. In contrast, in all of the clinical studies investigating TMLR-induced denervation using either positron-emission tomography or ^{123}Iodine MIBG-SPECT, comprising a total of 32 patients (including the 8 patients just previously mentioned), denervation was demonstrated in 67% to 100% of the patients that showed relief of angina. In our study of 8 patients, this result was highly significant ($p = 0.0005$), and denervation could be attributed to TMLR in 43 of 50 segments (86%) with decreased tracer uptake [5]. The occurrence of reinnervation in some patients at 1 year after TMLR has been reported in one clinical study, but we still found denervation for as much as 16 months postoperatively [5]. Interestingly the denervation hypothesis may explain the short-term and the long-term reduction in angina. Denervation obviously may diminish anginal complaints early after the procedure, but the concomitant improved exercise also may promote arteriogenesis through increased shear stress in pre-existing capillaries [4, 5]. Therefore, despite the minimal clinical evidence for improved perfusion and left ventricular function in the first year after TMLR, this mechanism of exercise-induced arteriogenesis may explain the reported long-term reduction in angina, even when myocardial reinnervation occurs some time after TMLR.

In conclusion, "Light and Ice Cream" beautifully paraphrases that transmyocardial laser revascularization can be performed with various lasers as well as with other devices.

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