Mechanism of TMR; The Debate Continues

Please see page 24 for the article by Reuthebuch et al. to which this Editorial pertains.

Clinical experience with transmyocardial laser revascularization has increased significantly over the last few years. Since several transmyocardial laser revascularization studies reported an apparent effect on the relief of angina\(^1\)\(^-\)\(^4\) and the FDA approved reimbursement of transmyocardial laser revascularization procedures in the USA, thousands of patients have been treated worldwide with different laser systems using a surgical (transmyocardial laser revascularization) or a percutaneous approach. However, the mechanisms underlying the apparent benefit are not yet fully elucidated and many studies report different potential mechanisms of action. In addition, the paper of Reuthebuch et al. published in this issue\(^5\) does not provide data which helps us to reach a consensus about one proposed mechanism of action. Contrary to the current belief of rapid loss of patency, they demonstrate long-term patency of the laser channels created by a CO\(_2\) laser by a contrast echocardiography technique.

Initially, Mirhoseini, a pioneer in transmyocardial laser revascularization procedures in the late 1970s, proposed the idea of direct myocardial perfusion from the left ventricle cavity with a laser, thus mimicking the reptilian physiology\(^6\). However, evidence of postprocedural patent laser channels has been conflicting. Apart from one post mortem case report showing some patent small tracts within a laser channel remnant 94 days post CO\(_2\) laser transmyocardial laser revascularization procedure\(^7\) others failed to show such patent channels. Postmortem analysis of a deceased transmyocardial laser revascularization patient 45 weeks after the transmyocardial laser revascularization procedure using a CO\(_2\) laser, showed no patent laser channels but channel remnants filled with fibrous scar\(^8\). These findings were substantiated by a report from Gassler et al.\(^9\), who investigated the hearts of three transmyocardial laser revascularization patients who died 3, 16 and 150 days after the CO\(_2\) laser procedure. In all the three patients no patent channels were found, nor were the channels lined with endothelium. At different time points the laser channels showed an inflammatory healing response with the formation of fibrinous network with abundant granulocytes and thrombocytes inside the channel and a more organized fibrous scar at a later time point. These data are consistent with several experimental studies that investigated the patency of the laser channels and the effect of transmyocardial laser revascularization on the myocardial perfusion using different energy sources\(^10,11\). These studies also did not show clear evidence of patent channels or channel derivatives large enough to adequately supply blood from the cavity to the ischaemic myocardium\(^11\). However, what the postmortem studies and an abundance of experimental studies did show was proof of a neovascularization around and inside the laser channel remnants. Consistently, the formation of a capillary network in and around the channel remnants and vascular growth of arterioles in the treated region has been reported. This angiogenic and vessel remodeling effect is believed to be a uniform response to an inflammatory reaction caused by the laser. Tissue interaction with high density pulsed laser light energy usually results in a thermal and photo-acoustic ablation process. During the natural healing response of these laser lesions inflammatory cells are mobilized and activated. The subsequent release of multiple angiogenic cytokines by the inflammatory cells promote angiogenesis and vascular remodelling.

One of the main questions remains whether this angiogenic response is sufficient to supply the ischaemic myocardium in order to explain the symptomatic benefit that the majority of transmyocardial laser revascularization patients experience. Unfortunately, most perfusion imaging studies have failed to show an adequate improvement in myocardial perfusion after a transmyocardial laser revascularization procedure\(^1,2,4,12,13\). Multiple theories have been proposed to answer this paradoxical effect of transmyocardial laser revascularization. (1) Our present perfusion imaging techniques are not sensitive enough to detect small but perhaps clinical relevant improvements in myocardial perfusion. (2) The angiogenic response is insignificant and therefore not measurable, and other mechanisms of transmyocardial laser revascularization are responsible for the beneficial palliative effect, such as denervation, scarring of the ischaemic region or a placebo effect\(^14,15\). The former theory may indeed be true. The currently...
available perfusion imaging techniques have a rather crude spatial resolution; coronary angiography 100–150 μm, SPECT 1 cm, MRI 3 mm, PET 1 cm. The method in the report of Rheuthebuch et al[5] is of a different order and seems to be very refined with a resolution of 10 μm. However, the discrepancy between human histology reports and the proof of patent channels reported in this issue by contrast echocardiography remains of interest. Furthermore, the main question still remains unanswered: whether the reported patent channels with their systolic blood flow from the left ventricle cavity towards the myocardium can indeed improve myocardial perfusion in rest and under stress conditions. We eagerly await further proof of long-term patent laser channels and proof of improved myocardial perfusion by transmyocardial laser revascularization.

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References