Myocardial Laser Revascularization

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CB, KH, RC

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Preface

Completeness of revascularization has long been a mainstay of the surgical treatment of coronary artery disease. This goal has become increasingly difficult with a marked rise in the number of patients that have severe diffuse coronary artery disease. While percutaneous interventions have certainly been successful in treating coronary lesions their impact has been to further skew the population of patients that are referred for surgery and stenting is also limited by diffuse coronary disease.

With these limitations of conventional revascularization, novel methods to improve myocardial blood flow and perfusion have been investigated. One of these methods that has demonstrated clinical success is transmyocardial laser revascularization (TMR). Initially based teleologically on the idea of the reptilian heart in which blood flows directly from the left ventricle into the myocardium, laser channels were created to mimic similar direct pathways. Experimental work has indicated that the principal mechanism for TMR may be the stimulation of new blood vessels rather than the creation of transmural channels. TMR has been demonstrated in multiple randomized controlled trials to provide symptom relief for patients with severe angina. Based on these findings with sole therapy TMR, combination use with coronary artery bypass grafting has also been performed.

The intent of this book is to provide the reader with a complete understanding of the indications, results, mechanisms, and limitations of transmyocardial laser revascularization. While our understanding and treatment of the macrocirculation of the heart is reasonably well understood, our grasp of the micro-circulation as evidenced by the clinical success of TMR is less axiomatic.

Charles Bridges
Keith Horvath
Ray Chiu
2006

CHAPTER 1

Scientific and historic precedents

OH Frazier, Marianne Bergheim, and Kamuran A Kadipasaoglu

Introduction

Transmyocardial laser revascularization (TMR) is based on anatomic and physiologic principles long known and accepted in the history of medicine. The coronary anatomy was first described accurately by Vesalius in his landmark 16th-century text, *De humani corporis fabrica* [1]. The anatomic pathway of the coronary circulation was further elucidated by Vieussens [2], the royal physician to Louis XIV [3]. Vieussens documented the presence of direct vascular communication between coronary arteries and the chambers of the heart [4]. In 1706, he published *Nouvelles découvertes sur le coeur*, which was recognized at the time as the most accurate and detailed account of the structure and function of the heart [5]. This work described the circulation of the heart as inferred from postmortem experiments on the hearts of humans, calves, and sheep [2,3]. In these studies, Vieussens ligated the vena cava and pulmonary veins and injected saffron dye dissolved in alcohol into the coronary arteries. Once injected, the dye solution not only followed the accepted anatomic conduit through the coronary sinus and into the right atrium, but also flowed directly into the right and left ventricular chambers through small channels in the walls of the atria and ventricles [6]. Vieussens labeled these ducts joining the ventricular cavities to the coronary arteries "ducti carnosi" [2,4].

Two years later in Leiden, Holland, Thebesius [7] published *De circulo sanguinis in corde*, also relating to the microanatomy of the myocardium. Thebesius discovered openings in the endocardium by injecting water into the coronary sinus and observing the subsequent arrival of effluent in the atria and ventricles. Further experiments in which air, colored liquids mixed with wax, and glue were injected into the coronary veins provided the same results, confirming the presence of the ducts in the cardiac chambers [4,6]. Thebesius and Vieussens described the same channels, Thebesius by injecting the veins and Vieussens by injecting the arteries. Although Vieussens first reported the existence of these openings, all myocardial vessels that connect to cardiac chambers are now called thebesian vessels. In any case, by the early 18th century, the unique character of the coronary circulation was well established.

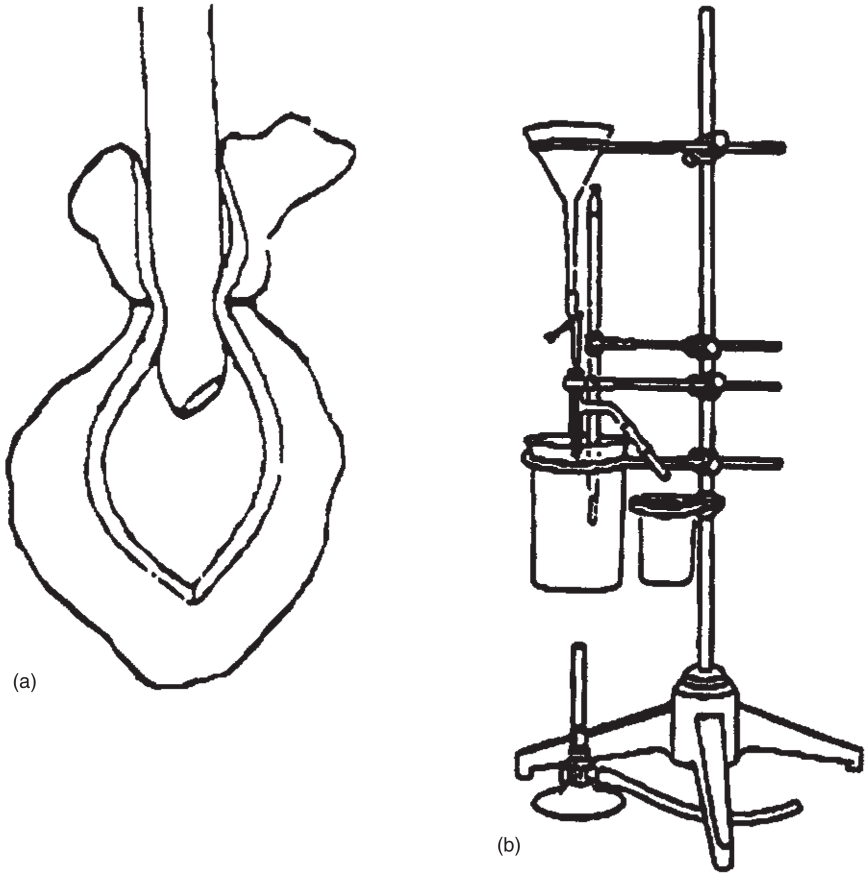
The study of comparative anatomy was popularized by the French anatomist Cuvier [8] in the late 18th and early 19th centuries. Cuvier described various ways that nature dealt with the problem of vascularizing the organ responsible for supplying blood to the rest of the body. As one moves up the evolutionary ladder, the circulation moves from one of direct perfusion from the ventricular cavity through the spongy, non-compacted myocardium as seen in fish and reptiles to one of direct coronary blood flow as seen in mammals. Interestingly, the various steps in this phylogenetic evolution of the coronary circulation are closely recapitulated in the development of the human embryo. Historically, the presence of this retained non-compacted myocardium contributing to a pathologic condition was first noted by Grant [9] in the 1920s. This abnormality, which may be seen in both symptomatic and asymptomatic patients [10,11], is appreciated more today because of the precise diagnostic capabilities of cardiac magnetic resonance imaging (MRI) and echocardiography.

The physiologic potential and possible functional importance of this direct ventriculomyocardial communication was demonstrated by a simple, yet ingenious, experiment by Pratt [12] in 1898. Pratt demonstrated that, by delivering defibrinated blood directly into the ventricular cavity and totally excluding the coronary circulation, it was still possible to maintain cardiac contractility and function, with the only source of oxygenated blood being directly through the ventricular myocardium. In this way, contractility was maintained in a mammalian model for several hours (Figure 1.1).

In 1928, while working in Boston's city morgue, Leary and Wearn [13] detailed the postmortem coronary circulation in two patients who had chronic syphilitic aortitis. Syphilitic aortitis had long been known to selectively invade the ascending aorta. In these two patients, the aortic origin of both coronary arteries had been chronically occluded by this disease. In spite of this, both patients were known to have maintained active lifestyles and gainful employment for a number of years before they died. This finding particularly intrigued Wearn and moved him to question how blood was able to reach the heart despite the obliteration of the coronary access.

After relocating to Western Reserve University in Cleveland, Wearn [6] embarked on a study to further elucidate this question. He studied human hearts by perfusing the coronary arteries with a celloidin mass too thick to enter the capillaries and subsequently observed celloidin plugs in the walls of the heart chambers, indicating that the celloidin had bypassed the capillaries. He detailed his findings in a paper published in 1933 [6]. Dissection and negative casting revealed direct vascular communication between the coronary arteries and the ventricular cavities via two types of vessels, identified as the arterioluminal and arteriosinusoidal vessels. Located near the endocardium, the arterioluminal vessels run directly from the coronary arteries into the lumen of the heart. The arteriosinusoidal vessels are small branches of coronary arteries that eventually lose their arterial character and divide into channels called myocardial sinusoids (Figure 1.2). Myocardial sinusoids vary in diameter from 50 to 250 µm and have thin walls consisting of endothelial tissue.

The study of myocardial circulation became much more pertinent throughout the 1920s and into the 1930s, as angina and coronary artery disease in general became increasingly observed clinically. Nevertheless, the treatment



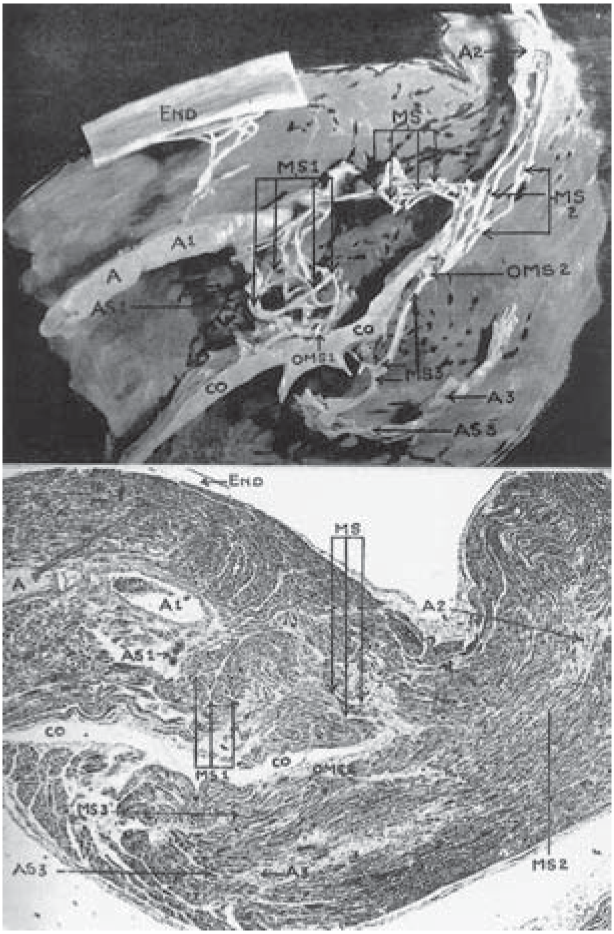
(a) (b)

Figure 1.1 (a) Diagram illustrating cannulation of right ventricle of feline heart for perfusion through thebesian veins. (b) This apparatus perfused the feline heart with defibrinated blood through the ventricles and maintained myocardial contractility for several hours. From Pratt [12] with permission.

options for coronary artery disease in this era were limited to symptomatic therapies such as nitroglycerin, which reduced or palliated anginal symptoms.

Claude Beck [14–20], who had been a surgeon in Boston and had also moved to Western Reserve University School of Medicine in Cleveland, was aware of the work of Wearn and was intrigued by his observations regarding the microcirculation of the heart. Beck had also observed extensive collateral blood supply accompanying the restrictive pericarditis frequently associated with tuberculosis. To Beck this seemed to imply that augmentation of blood supply was being induced by an inflammatory response to this infectious process. The possibility implied by Wearn's work was that this augmented blood supply might reach the myocardium directly, thereby bypassing the occluded coronary arteries. Beck attempted to produce this response by irritating the myocardium through abrasion and introduction of foreign bodies (talc) [14,15].

(a)



(b)

Figure 1.2 (a) Wax reconstruction revealing direct communication between coronary arteries and left ventricle via arterioluminal and arteriosinusoidal vessels. (b) Serial section from block of myocardium used to create the wax reconstruction shown in top panel (magnification ×41). A, artery; AS, arteriosinusoidal vessel; CO, common opening; END, endocardium; MS, myocardial sinusoid; OMS, opening of a myocardial sinusoid into ventricular lumen. From Wearn *et al*. [6] with permission.

The historic demonstrations of Vieussens and Thebesius implied that direct arterial blood could be brought to the ischemic myocardium by utilizing the venous system. Beck decided to bring arterial blood to the ischemic myocardium in the same way. This approach was once again based on the extensive interconnecting microcirculatory network that proliferated in response to myocardial ischemia. Beck utilized the brachial artery as a graft and the coronary sinus as a conduit from the descending aorta. This operation was researched extensively in the experimental animal and first applied to patients in 1948 [17]. The intrepid Beck performed this milestone operation without benefit of today's modern vascular instruments or suture materials and, more importantly, without access to cardiopulmonary bypass. This retrograde bypass was performed 20 years before the introduction of antegrade coronary artery bypass procedures. Beck combined various approaches to this indirect revascularization, utilizing chemical and mechanical means to enhance anastomotic channels through adhesions combined, in some cases, with arterialization of the coronary sinus [14–20]. Despite a high mortality rate for these procedures, Beck reported relief of anginal symptoms in the majority of patients [17–20].

Taking an even more direct approach to myocardial revascularization, the Canadian surgeon Vineberg [21,22] began implanting the internal mammary artery (IMA) into the left ventricular wall of canine hearts in 1945. This direct myocardial revascularization technique took advantage of the sponge-like character of the myocardial sinusoids, thus allowing direct communication between the IMA implant and myocardial cells. Postoperative studies confirmed microscopic anastomosis between the open IMA graft and the arteriolar branches of the poorly functioning canine coronary artery. Vineberg performed this procedure for the first time on a patient with coronary insufficiency in 1950 [22]. The majority of patients reported improvement in anginal symptoms as well as increased duration of physical activity. Vineberg's angiographic demonstration of the patency of the open IMA graft, as well as extensive communication to the microcirculation of the heart, enhanced the credibility of these anecdotal reports. The introduction of cardiopulmonary bypass, as well as improvements in vascular instruments and suture materials, allowed coronary artery bypass grafting (CABG) to supplant the Vineberg procedure by the late 1960s. Nevertheless, in 1975, Vineberg [23] demonstrated the long-term effectiveness of the IMA graft procedure when he reported the continued patency of the arteriomyocardial connections and the important symptomatic relief afforded by the procedure after 24 years of follow-up (Figure 1.3). The report included 94 patients, with 84% showing graft patency.

Following Goldman *et al.*'s proposal [24] in 1957 to create a direct communication between the ventricular cavity and coronary circulation using straight and U-shaped arterial grafts, Massimo and Boffi [25] initiated the use of T-shaped polyethylene tubes to offer more protection against obstruction caused by compression during myocardial contractions. That same year, Massimo and Boffi reported that the T-shaped tubes successfully delivered oxygenated blood from the left ventricle directly into the ischemic myocardium of dogs.

In 1964, before CABG had become generally accepted, Sen *et al.* [26–28] reported the use of a unique method of direct revascularization. They based their approach on the accepted corollary, established by Wearn, Pratt, Vineberg, and others, that myocardial viability is preserved by the proliferation of the microcirculation. The aim was to enhance blood flow to the ischemic myocardium by creating small channels with a large-bore needle directly from the left ventricle to the myocardium. Sen noted that Cooley had described to him, in a personal communication, Cooley's use of transmyocardial acupuncture in several desperate cases of insufficient myocardial perfusion in the 1960s [27]. Sen

(a)

(b)

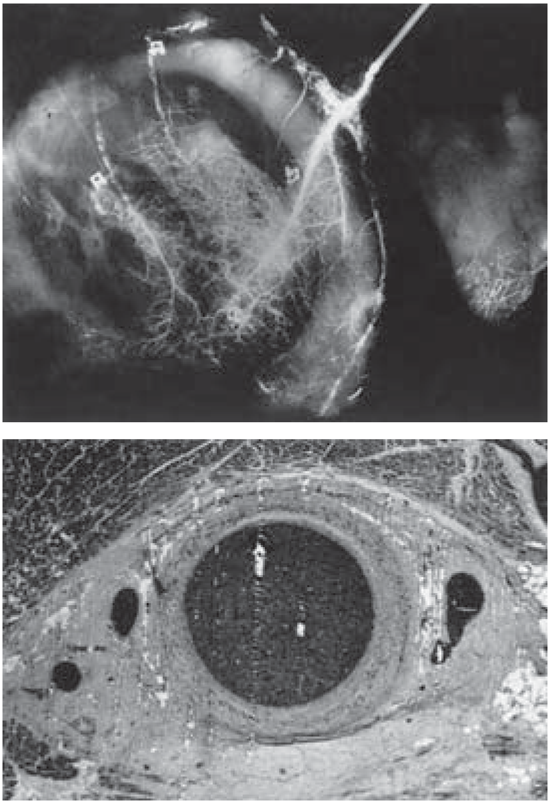


Figure 1.3 Internal mammary artery (IMA) graft after 24-year follow-up. (a) Radiograph of left myocardial network injected with contrast agent to demonstrate graft patency. (b) Histopathologic section of patent IMA graft. From Vineberg [23] with permission.

speculated that the transmyocardial channels would facilitate blood flow to the bed made more receptive of this flow by the proliferation of the microcirculation in response to chronic myocardial ischemia. Creation of this alternate route of blood flow was an attempt to duplicate the reptilian circulation (Figure 1.4). In the reptile, the coronary arteries are small, perfusing less than one-tenth of the myocardial thickness, and most of the myocardium is supplied directly from the ventricular cavity to the myocardial sinusoids during systolic contraction. This attempt by Sen to improve myocardial perfusion through direct ventriculo-myocardial communication was an early clinical application of transmyocardial revascularization (TMR) [28].

In 1967, while performing a Vineberg procedure on a 61-year-old man with triple coronary artery disease, Hershey and White [29] employed Sen's acupuncture technique as a last resort to save the patient from refractory ventricular fibrillation. After puncturing the left ventricle approximately 100 times with a 2.5-mm intravenous knobbed cannula and applying prolonged intermit-