Options for the “No-Option” Refractory Angina Patient

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As mortality from coronary artery disease (CAD) has declined, an increasing number of patients develop advanced CAD with ongoing angina not amenable to percutaneous or surgical revascularization. Many have refractory angina despite optimal medical therapy and have been labeled “no-option” patients.1 Overlap between clinical symptoms, myocardial perfusion abnormalities and coronary anatomy for these patients can be very complex and frequently requires an individualized treatment approach.

Until recently, there was limited data on the natural history of refractory angina. In a recent series of 500 consecutive patients undergoing cardiac catheterization, 16 percent had significant CAD and were suboptimal candidates for revascularization and seven percent were truly “no-option” patients.1 In the United States, an estimated 12 million patients have chronic angina and as many as 1.8 million may have refractory angina.1

Early mortality following diagnosis was assumed for refractory angina patients. However, a recent study of 1,200 patients from a dedicated refractory angina clinic reported a low annual mortality rate of only 3 to 4 percent (Fig. 1).2 Therefore, a major focus of care for this population has become quality of life in the face of debilitating symptoms and increased healthcare utilization (i.e., hospital admission). To meet the needs of this complex patient group, specialized clinics are being developed that use a multidisciplinary approach.

In the past, treatment options for patients with refractory angina were limited to traditional anti-anginal therapy and secondary risk-factor modification. Alternative strategies have recently been developed, including novel pharmacological agents, enhanced external counterpulsation (EECP®), shock wave therapy, neuromodulation, and others.

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Figure 1: Kaplan-Meier survival curve in 1,200 patients with refractory angina; center line is the estimated fraction surviving, upper and lower lines are 95 percent pointwise confidence intervals. Originally published in the European Heart Journal (Oxford University Press) on behalf of the European Society of Cardiology.
myocardial angiogenesis using stem cell therapy and novel interventional techniques (aggressive treatment of chronic total occlusions and reduction of the coronary sinus).

Novel pharmacologic options—including nicorandil, ivabradine and perhexiline—are used throughout the world but are not available in the United States. L-Arginine (6 to 9 grams daily) has been shown to improve coronary blood flow via nitric oxide-mediated endothelium-dependent vasodilation and may improve symptoms in select patients. Ranolazine affects ion channels by inhibiting late sodium currents and has demonstrated efficacy in patients with stable angina. Ranolazine (500 mg twice daily, increasing to 1,000 mg twice daily) also appears effective in refractory angina patients, although 15 to 25 percent of individuals will experience either inadequate clinical benefit or side effects.

EECP is a noninvasive technique that simulates the action of an intra-aortic balloon pump. Three pairs of pneumatic blood pressure cuffs are placed on the legs. The cuffs inflate distal to proximal during diastole and deflate during systole (Fig. 2). The MUST-EECP trial demonstrated significant improvements in time to exercise-induced ST depression and angina. Proposed mechanisms of benefit include recruitment of collateral vessels via activation of growth factors, improvement of endothelial function and a peripheral training effect. EECP also increases nitric oxide and circulating CD34+ cells. A standard course of EECP is 35 one-hour sessions over seven weeks; twice-per-day sessions are also prescribed.

Chronic total occlusions (CTOs) can be successfully recanalized in up to 90 percent of appropriately selected patients using novel antegrade and retrograde techniques with improvement in symptoms. Recently, a unique stent, the Neovasc Reducer™ placed in the coronary sinus has been shown to decrease angina in patients with Class 3–4 symptoms (Fig. 3). Preclinical data indicates cell therapy can promote neovascularization, thus improving myocardial perfusion and function. Cell therapy exerts paracrine effects, mobilizing both resident and circulating stem cells. A recent meta-analysis in patients with either ischemic heart failure or refractory angina who were not candidates for revascularization found that cell therapy–treated patients demonstrated improvements in angina, exercise tolerance and mortality. CD34+ cells appeared particularly promising. A multicenter, placebo-controlled Phase 2 trial showed durable improvements in angina and exercise time.

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Neuromodulation is the use of chemical, mechanical or electrical means to interrupt pain signals anywhere in the transmission pathway from the periphery to the brain. Spinal cord stimulation has been used for decades in a variety of chronic pain syndromes and is the treatment of choice in patients with no option of revascularization. Neuromodulation has been used for five decades in a variety of chronic pain syndromes and is the treatment of choice in patients with no option of revascularization. Neuromodulation is the use of chemical, mechanical or electrical means to interrupt pain signals anywhere in the transmission pathway from the periphery to the brain. Spinal cord stimulation has been used for decades in a variety of chronic pain syndromes and is the treatment of choice in patients with no option of revascularization. Neuromodulation has been used for five decades in a variety of chronic pain syndromes and is the treatment of choice in patients with no option of revascularization.

**References**

A Hybrid Approach to the Treatment of Congenital Heart Disease
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Advances in the treatment of congenital heart disease have had a remarkable impact on survival, with 89 percent of people born in the 1990s with congenital heart disease now living into adulthood. As a result, congenital heart programs are facing a significant challenge: how to best care for the adult patients, who will continue to require specialized treatment for the entirety of their lives.

At Cedars-Sinai, congenital heart patients are being maintained in the same medical home throughout their lives, without the need to transition to a new program or team of physicians when they age out of pediatric care. By keeping patients within the same core group of congenital heart specialists, we hope to develop lifelong treatment plans that will have a positive impact on longitudinal outcomes.

Another overarching tenet for our program is a team approach with concurrent management of each patient by an interventional congenital cardiologist and a congenital heart surgeon, with a wide range of additional specialists available for consultation as medically necessary.

Case Study: Hybrid Surgery Reduces Impact

By joining interventional cardiology and congenital heart surgery, we are working to develop a hybrid approach to congenital heart care that lessens the impact of repeated surgeries on congenital heart patients. One such example is a periventricular placement of a Melody® valve in a patient with tetralogy of Fallot with a native outflow tract.

Presently, there are more than 100,000 patients with tetralogy of Fallot. The criteria for re-operation on these patients, mostly for pulmonary valve replacement, is in the process of being redefined. It was once believed that a patient with repaired tetralogy of Fallot would not need another operation. However, it has become apparent that a portion of these patients will require placement of a pulmonary valve in order to prevent the negative effects of chronic regurgitation of blood into the right ventricle, caused by resecting the abnormal pulmonary valve and in most cases placing a patch to increase the size of the right ventricular outflow tract (RVOT patch). We are now finding that a much higher percentage of individuals are candidates for re-operation than expected: 75 to 100 percent of patients with repair of tetralogy of Fallot and significant pulmonary insufficiency may benefit from placement of a competent valve.

There are two primary approaches to placement of a pulmonary valve. The gold standard is surgical replacement of the valve. The valve can be placed with very little morbidity and mortality, but requires open-heart surgery and using cardiopulmonary bypass. Other medical issues, such as pulmonary artery stenosis, arrhythmias and residual shunts, can be addressed at the same time.

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Figure 1: Three-dimensional model (left) of the patient’s reconstructed right ventricular outflow tract and pulmonary arteries, which was used to develop the technique and simulate the planned procedure; and intraoperative angiograms (right) showing actual wire and stent position. Each stage was accurately predicted by using the model: wire placement (A), stent placement—10 mm covered stent and 30 mm Palmaz (B) and final result (C).
In recent years, percutaneous valve replacement has emerged as an alternative to open-heart surgery, offering an overall decreased impact to the patient. This approach is only for patients with previous conduit placement during their repair, approximately 15 percent of all tetralogy of Fallot patients. Other heart issues cannot be addressed during the procedure.

Combining the benefits of both open heart and percutaneous procedures is the hybrid approach. This hybrid approach was used in a 16-year-old boy who was referred for traditional pulmonary valve replacement at another hospital and was found not to be a candidate for a percutaneous valve replacement. Like most patients in this situation, he had originally been led to believe he would not need another surgery, and he was very fearful about having his chest reopened. The patient and family came to Cedars-Sinai looking for a less invasive approach.

After evaluating the patient and his underlying medical condition, we felt he was an ideal candidate for a novel hybrid approach for placement of a pulmonary valve. We used his MRI scan to make a three-dimensional reconstruction of his right ventricle and outflow tract. The model served to simulate the approach that we would use, thus avoiding the need for bypass (Fig. 1). Using the model, we were able to precisely determine the exact wire position, sequence of steps, and appropriate stent placement. The patient did very well and was discharged from the hospital the next day with a competent valve. He should not need any further surgical interventions.

A Team Approach to Care

Our success with novel, collaborative, hybrid surgeries (exemplified by the above case) has reinforced our program’s commitment to communication and teamwork in all aspects of patient care.

Team decision-making begins with daily rounds: physicians, nurses, respiratory therapists, child life specialists, nursing leadership and pharmacists rounding together, with other specialists involved depending on specific needs of the patient. For a neonatal patient, the neonatologist and neonatal nurses who are caring for the patient on a daily basis join the team. For an adult patient, adult-care nurses and intensivists join us.

In the congenital heart operating room, we have at least nine healthcare providers actively involved in the management of the patient. These providers include surgeons, pediatric cardiac anesthesiologists, cardiologists, congenital perfusionists and specialized operating room nurses.

A multipronged strategy ensures everyone on the team understands the goals and the expectations for each patient:

- A preoperative briefing report outlines the patient’s medical condition and history, perfusion technique to be used, operative sequence, equipment needs, blood bank needs, lines needed, and the expected surgical plan. The report is distributed the day before the procedure.
- Team huddle the morning of the surgery allows us to review together the patient condition, surgery, anesthesia, perfusion, nursing goals and equipment needs (Fig. 2).
- The postoperative hand-off to the ICU team is conducted in accordance with the AHA scientific statement on improving communication in the cardiac operating room.

In developing the congenital heart program at Cedars-Sinai, we felt it was imperative to employ such a team approach. Drawing inspiration from the collaboration required between surgeon and interventional cardiologist for the new generation of hybrid surgical procedures, we refer to our overall management style as the “hybrid thought process.” It is our hope that the habits of communication and teamwork built into our program will continue to foster novel, hybrid approaches to patient care.

References


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