The tragedies of life are largely arterial.
—Sir William Osler

The term “acute aortic syndrome” encompasses diverse catastrophic events affecting the aorta that require prompt diagnosis, triage and treatment. These include aneurysmal aortic rupture, symptomatic intramural aortic hematoma, symptomatic penetrating atherosclerotic ulcer, traumatic aortic transection, and acute type A and B aortic dissection. Acute aortic syndrome is among the most challenging conditions encountered in the hospital setting. Acute aortic syndrome is about a hundred times deadlier than acute coronary syndrome, and the diagnosis may be delayed in up to 40 percent of affected patients.1

An open surgical approach has been the standard of care for various aortic pathologies since the 1950s, and remains so for a selected cohort of patients.

Since the emergence of thoracic endovascular aortic repair (TEVAR) as an alternative option, the treatment algorithm has changed dramatically. TEVAR avoids morbid thoracotomy and thoracoabdominal incisions, cardiopulmonary bypass, aortic cross-clamping and hypothermic circulatory arrest.

In TEVAR procedures, the patient’s peripheral arteries, such as the femoral, axillary and carotid arteries, are used to deliver the stent graft to the diseased area of the aorta. The majority of TEVAR patients at Cedars-Sinai undergo a percutaneous procedure using the Perclose® ProGlide™ technique, a minimally invasive method that does not require surgical exposure of the peripheral arteries.

This article overviews treatment considerations for two common aortic pathologies of the descending thoracic aorta: aortic aneurysm and acute type B aortic dissection.

Continued on page 2 (see “Aortic”)
Aortic: continued from page 1

Descending thoracic aortic aneurysms

The multicenter trial leading to the first FDA-approved stent graft involved 139 patients with underlying descending thoracic aortic aneurysm. TEVAR patients were compared to similar patients treated with open operation (n=96). The results of this study, which involved the Gore TAG stent graft, were pivotal in changing the primary treatment modality in the descending thoracic aorta. The TEVAR procedure reduced mortality from 9 to 2 percent and paraplegia from 14 to 3 percent. The length of ICU stay among the TEVAR group was 50 percent of the open group.

Two other U.S. trials involving the Medtronic Talent and the Cook TX2 stent graft have confirmed the feasibility and safety of TEVAR for patients with fusiform descending thoracic aortic aneurysm and symptomatic aortic ulcers. The caveats with the endovascular approach remain the higher re-intervention rate, mostly due to endoleaks, and the need for postoperative surveillance imaging.

Cedars-Sinai is one of the top three enrolling sites for the THRIVE phase IV clinical trial offering TEVAR to patients with thoracic aneurysm or penetrating ulcers. The Cedars-Sinai Heart Institute’s higher-risk patients with descending thoracic aortic aneurysm and cardiac and pulmonary comorbidities are offered TEVAR.

Younger patients, however, are recommended open operation to avoid potential long-term consequences of contrast and radiation exposure, especially if they are not good anatomic candidates for TEVAR. The majority of patients with connective tissue disorders, such as Marfan, Ehlers-Danlos and Loey-Dietz syndromes, are also offered open operations given the concerns of repair durability due to enlargement of proximal and distal landing zones. However, some such patients presenting in extremis are offered lifesaving TEVAR because the procedure is less invasive and better tolerated in very sick patient cohorts. As part of the informed consent in this patient population, it is important to make clear that future open replacements are very probable.

Type B aortic dissection

The majority of patients with uncomplicated type B aortic dissection can be treated conservatively with anti-impulsive therapy. However, up to 20 percent of these patients can present with or later experience severe complications, such as rupture, impending rupture, or branch- vessel malperfusion. These challenging patients are usually triaged to surgical or endovascular management.

The surgical approach was the standard of care for the treatment of complicated type B aortic dissection in the last four decades. Surgical management has been challenging, even in centers of excellence. Coselli and co-authors reported their results with surgical management of acute type B aortic dissection. With an in-hospital mortality of 22.4 percent, they observed the lowest death rate of any published series. In contrast, our retrospective analysis of patients with acute complicated type B aortic dissection treated with TEVAR had a favorable 11 percent (n=3) in-hospital mortality. The survival curve after three-year follow-up compared very favorably to surgical results, and 85 percent of TEVAR patients underwent reverse aortic remodeling.

For these reasons, TEVAR of acute aortic dissection has gained increasing interest as an initial treatment option for patients with complicated type B aortic dissection. The goal of TEVAR is to exclude the primary entry site, obliterate the false lumen, prevent aortic rupture and relieve lower body malperfusion. Cedars-Sinai is one of the 12 enrolling sites in the Valiant® Complicated Type B Aortic Dissection Trial in the U.S. This study is considered pivotal for dissection-specific FDA approval.

Our aortic specialists perform the majority of the TEVARs using intravascular ultrasound (IVUS). IVUS allows for more detailed luminal interrogation while reducing contrast and radiation to the patients and health care providers. In patients with advanced renal dysfunction (glomerular filtration rate below 50 mL/min/1.73 m²), the imaging of the entire TEVAR procedure is performed using IVUS and fluoroscopy to avoid any contrast-induced nephropathy.

In summary, endovascular repair has revolutionized our approach to various aortic pathologies. A sicker patient population can now undergo a percutaneous procedure and expect a quicker recovery. Yet open aortic operations are here to stay, as they offer proven longevity and superior efficacy in patients with connective tissue disorders. This article concludes with a quote from the godfather of stent graft therapeutics:

“The aortic treatment is best provided by specialists who can provide both open surgical and endovascular therapies.”

— Juan Parodi, MD

Dr. Khoynezhad is an Associate Professor of Surgery and Director of Thoracic Aortic Surgery at the Cedars-Sinai Heart Institute. Ali.Khoynezhad@cshs.org.

* Some of the human research activities described in this article were initiated at non-Cedars-Sinai institutions prior to the investigator’s arrival at Cedars-Sinai.

For references, please see page 4.
Noninvasive Fractional Flow Reserve: Assessment of Lesion-Specific Ischemia Derived from CCTA

James K. Min, MD

Since the introduction of 64-detector row computed tomography (CT) scanners in 2005, coronary CT angiography (CCTA) has emerged as a promising noninvasive anatomic method for producing high-resolution, motion-free images of the coronary arteries in patients with suspected coronary artery disease (CAD). Numerous early studies evaluated the diagnostic accuracy of CCTA, generally employing a >50 or a >70 percent luminal diameter stenosis as a threshold of “significant” CAD and using quantitative assessment by catheter-based angiography as a reference standard. These studies demonstrated consistently high diagnostic performance of CCTA as compared to invasive angiography, with per-patient sensitivities and specificities ranging from 91–99 percent and 74–96 percent, respectively (Fig. 1); but were influenced by a number of potential mitigating factors, including referral, spectrum, work-up and publication biases.

The ACCURACY trial was performed to address many of these limitations.1 This trial was the first prospective multicenter study to directly compare CCTA to quantitative catheter-based angiography in 230 consecutive patients without known CAD referred for invasive angiography for clinical indications. Despite clinical suspicion of significant anatomic CAD, only 13.9 percent of study patients were found to have obstructive CAD at the >70 percent stenosis threshold. At this low to intermediate prevalence of anatomically obstructive CAD, the diagnostic sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) was 94, 83, 48 and 99 percent, respectively. CCTA further demonstrated high discriminatory power with an area under the receiver operating characteristics curve (AUC) of 0.95. A subsequent prospective multicenter European study of 360 patients without known CAD revealed similarly high diagnostic performance of CCTA at a higher prevalence of obstructive CAD (68%).2 In this cohort, CCTA displayed a sensitivity, specificity, PPV and NPV of 99, 64, 86 and 97 percent respectively—confirming the utility of CCTA for identification of high-grade coronary artery stenoses in individuals with suspected but without known CAD across a wide range of disease prevalences, in particular for the exclusion of significant coronary stenoses.

Despite the robustness of CCTA to exclude significant coronary artery stenoses, the less-than-perfect specificity of CCTA has raised concerns that a systematic bias towards overestimation of coronary stenosis severity may exist, and might result in unnecessary referral of patients to invasive angiography for non-high-grade lesions. Further, the “significance” of coronary lesions judged by an anatomic stenosis severity threshold alone has recently been challenged by several large-scale randomized trials—including the COURAGE and BARI 2D trials, which revealed no improvement in event-free survival in patients treated with optimal medical therapy (OMT) and coronary revascularization based upon anatomic thresholds as compared to OMT alone.3,4 In contrast, the FAME trial revealed the importance of assessing lesion-specific ischemia by fractional flow reserve (FFR), an invasive method for determining the hemodynamic significance of a coronary lesion(s), and defined as the ratio of maximal blood flow in a stenotic vessel to the blood flow in the hypothetical case that the artery was normal.5 Use of FFR as a physiologic adjunct to anatomic stenosis severity has proven effective to guide decisions of coronary revascularization, and this combined anatomic-physiologic approach to CAD assessment results in near- and intermediate-term event-free survival, reduces unnecessary revascularization and lowers CAD-related costs.

In this regard, recent investigations have evaluated the feasibility of computation of FFR from static CCTA image data to allow for a combined anatomic-physiologic assessment of CAD by a noninvasive method. Significant advances in the field of computational fluid dynamics (CFD)—which have been utilized in the fields of aeronautical and automotive engineering for decades—have been instrumental to permit physiologic modeling using cardiovascular image data, employing supercomputers that solve for equations of coronary blood flow and pressure. Derivation of FFR from CCTA data (FFRCT) allows for computation of both rest and hyperemic blood flow and pressure in a manner similar to invasive techniques, and importantly, does not require modification of CCTA imaging parameters, additional image acquisition or administration of medications.

The diagnostic performance of FFRCT was recently tested in the DISCOVER-FLOW study and reported at the EuroPCR 2011.6 This four-center study enrolled 103 stable patients with suspected or known CAD and suspected anatomic stenosis by CCTA who were referred for clinically indicated invasive angiography and FFR. In keeping with prior multicenter trials, obstructive CAD by CCTA and invasive angiography was defined by a >50 percent luminal diameter stenosis, while lesion-specific ischemia was defined as an FFR or FFRCT <0.80. Amongst the 159 vessels interrogated by invasive FFR, the majority was of the left anterior descending artery (n=87), followed by the left circumflex artery (n=41) and right coronary artery (n=31) [Fig. 2-3]. Compared to CCTA obstructive CAD alone, FFRCT demonstrated similar sensitivity (88% vs. 91%) and NPV (92% vs. 89%), but significantly higher specificity (82% vs. 40%) and PPV (74% vs. 47%), which resulted in a marked 25 percent improvement in overall diagnostic accuracy (84% vs. 59%). Similar results were observed for the per-patient analysis, and were driven by a 70 percent reduction in false positive diagnoses by the FFRCT. The discriminatory power for lesion-specific ischemia for FFRCT was also superior to CCTA stenosis severity (AUC 0.90 vs. 0.75), with no improvement in the diagnosis of lesion-specific ischemia when CCTA stenosis was added to FFRCT (AUC 0.91). The overall correlation of FFRCT to invasive FFR was

Continued on page 4 (see “CCTA”)
This study has been designed to examine the per-patient diagnostic performance of FFR_{CT} for the detection and exclusion of lesion-specific ischemia. With enrollment nearing completion, DeFACTO will be the definitive study to determine the diagnostic performance of this novel technology, and results from DeFACTO are expected to be available in early 2012. 7

In the past six years since the clinical introduction of CCTA, several prospective multicenter trials have established the high diagnostic performance of CCTA for the diagnosis of anatomically obstructive CAD. The potential additive utility of CCTA for the physiologic assessment of lesion-specific ischemia is currently being tested by the novel FFR_{CT} technology, and its introduction to daily clinical cardiac care may provide a combined noninvasive method for anatomic-physiologic assessment of CAD in a lesion-specific manner. This may help guide physicians as they make decisions related to medical therapy and coronary revascularization.

References:

6. EuroPCR 2011 Scientific Sessions
7. Clinicaltrials.gov: NCT01233518

Khoynezhad References: