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THE PRESENT AND FUTURE

REVIEW TOPIC OF THE WEEK: POINT

Alcohol Septal Ablation for Obstructive Hypertrophic Cardiomyopathy

A Word of Endorsement

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ABSTRACT

Twenty years after the introduction of alcohol septal ablation (ASA) for the treatment of obstructive hypertrophic cardiomyopathy, the arrhythmogenicity of the ablation scar appears to be overemphasized. When systematically reviewing all studies comparing ASA with myectomy with long-term follow-up, (aborted) sudden cardiac death and mortality rates were found to be similarly low. The focus should instead shift toward lowering the rate of reinterventions and pacemaker implantations following ASA because, in this area, ASA still seems inferior to myectomy. Part of the reason for this difference is that ASA is limited by the route of the septal perforators, whereas myectomy is not. Improvement may be achieved by: 1) confining ASA to hypertrophic cardiomyopathy centers of excellence with high operator volumes; 2) improving patient selection using multidisciplinary heart teams; 3) use of (3-dimensional) myocardial contrast echocardiography for selecting the correct septal (sub)branch; and 4) use of appropriate amounts of alcohol for ASA. (J Am Coll Cardiol 2017;70:481–8) © 2017 by the American College of Cardiology Foundation.

Hypertrophic cardiomyopathy (HCM) is the most common inheritable cardiac disease, present in 1 in 500 of the general population (1). Approximately two-thirds of patients with HCM have a significant gradient across the left ventricular outflow tract (LVOT) at rest or during physiological provocation and are classified as having *obstructive* HCM (2). First-line treatment in patients with significant LVOT obstruction is with negative inotropic drugs (beta-blockers, verapamil, and disopyramide) (3,4). In the 5% to 10% of patients who remain highly symptomatic despite optimal medical therapy, septal reduction therapy is indicated, either by surgical myectomy or alcohol septal ablation (ASA) (3–5).

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HISTORY OF SEPTAL REDUCTION THERAPY

First performed by Cleland in 1958, surgical myectomy was the first invasive treatment for obstructive HCM (6). Starting from 1960, Morrow used a technique in which a small, rectangular bar of muscle from just below the aortic valve to beyond the site of mitral-septal contact was resected. The results of the first 83 patients treated with this "Morrow procedure" were published in 1975 (7). Since then, numerous different surgical techniques have come and gone. The objective of most of these procedures was enlargement of the LVOT by means of myectomy to eliminate the systolic anterior motion of the anterior mitral valve leaflet and thereby reduce outflow obstruction. Mitral valve plication, extension, and replacement have also been proposed as alternatives to myectomy, and performed in selected patients (8,9).

At the end of the 1980s, an interventional approach to septal reduction began to take shape. Brugada et al. (10) were the first to treat a patient by injecting absolute alcohol into a septal branch of the left anterior descending artery. Their goal was not to treat

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ABBREVIATIONS AND ACRONYMS

ASA = alcohol septal ablation

HCM = hypertrophic cardiomyopathy

LVOT = left ventricular outflow tract

MCE = myocardial contrast echocardiography

NYHA = New York Heart Association

LVOT obstruction, however, but chemical ablation of ventricular tachycardia. The idea of reducing LVOT obstruction by a catheter-based method stems from the observation that myocardial function of selected areas of the left ventricle can be suppressed by balloon occlusion of the supplying coronary artery during angioplasty (11). In the years following the chemical ablation procedure reported by Brugada et al. (10), 2 groups of researchers almost simultaneously developed ASA for the treatment of obstructive HCM. Gietzen et al. (12) presented their preliminary findings at the Annual Congress of the German Cardiac Society in April 1994, and Sigwart presented his results at the Royal Brompton Hospital in London in June 1994 and subsequently published the first 3 cases in *The Lancet* (13).

NEEDLE VERSUS KNIFE

Since its introduction, there has been a polarizing debate concerning the role of ASA in the management of obstructive HCM. Publications from the "surgical side" of the discussion are characterized by recycling of selected (early) outcomes of ASA, whereas the "interventional side" frequently disregards the limitations of ASA. Ideally, a randomized controlled trial should be set up to end the discussion about which procedure is best. This would require 1,200 patients eligible and willing to be randomized to a percutaneous or surgical procedure. Because the prevalence of HCM is 1 in 500 and <10% of these patients require septal reduction therapy, such a trial is practically impossible, as Olivotto et al. (14) clearly demonstrated. Hence the only way to compare the 2 techniques at this time is by retrospective analyses.

STUDIES COMPARING ASA WITH SURGICAL MYECTOMY. ASA had to come of age, and the first substantial comparison with surgical myectomy was reported in 2010 by Agarwal et al. (15). In this meta-analysis, 12 studies comparing techniques were included. The most important limitation of this analysis was the short follow-up duration of the included studies (longest median follow-up 2.2 years), thus prohibiting the investigators from making statements on long-term outcomes. The meta-analysis we performed in 2015 therefore only included studies with a follow-up of at least 3 years (16). Remarkably, only 6 studies comparing ASA with myectomy were identified (**Table 1**) (17–22). In contrast, 44 studies were found describing the outcomes of 1 of the 2 interventions (16), a finding that may also be seen as a sign of the ongoing polarization.

In 2010, ten Cate et al. (17) conducted the first of the 6 studies comparing long-term outcomes of ASA and myectomy head to head. This study (subtitled "A Word of Caution") is the only study to date that reported a worse outcome following ASA compared with myectomy and is therefore frequently used (>100 citations) by opponents of ASA. Two years later, Sorajja et al. (18), from the Mayo Clinic in Rochester, Minnesota, compared ASA with myectomy by matching patients in a 1:1 fashion. The survival of ASA-treated patients was found to be comparable to the age-and sex-matched general population and to age- and sex-matched myectomy-treated patients. Steggerda et al. (19) compared ASA-treated patients with myectomy-treated patients, focusing on periprocedural complications and clinical efficacy. The same patients were also included in the largest study of its kind, by Vriesendorp et al. (20), which included 1,047 patients with HCM. During a mean follow-up of 7.6 years, survival after ASA or myectomy was found to be similar and comparable to that of patients with nonobstructive HCM. Finally, Samardhi et al. (21) and Sedehi et al. (22) described outcomes of relatively small groups of patients after ASA and compared these with outcomes following myectomy.

Of the 50 studies found by the systematic review (16), 24 studies were selected for meta-analysis, containing 16 myectomy cohorts (n = 2,791; mean follow-up 7.4 years) and 11 ASA cohorts (n = 2,013; mean follow-up 6.2 years). When we repeated the same search for studies published from 2015 to 2016, we only found 1 additional study, by Yang et al. (23), comparing long-term outcomes following the 2 procedures (**Table 1**).

LONG-TERM OUTCOMES. The initial performance of ASA was shrouded in safety concerns because of the intracoronary injection of cardiotoxic ethanol, creating a potentially arrhythmogenic ablation scar. However, all but 1 of the aforementioned studies showed similar mortality rates after ASA and myectomy despite the more advanced age of most of the ASA cohorts (**Table 1**) (15,16,18–23). Annual sudden cardiac death rates (including appropriate implantable cardioverter-defibrillator discharge) following ASA were also found to be similar to those in post-myectomy patients, ranging from 0.4% to 1.3%, when including unknown deaths (**Table 1**) (16,18,20,21).

The primary endpoint of the study by ten Cate et al. (17) was an unusual composite of cardiac death, aborted sudden cardiac death, and appropriate implantable cardioverter-defibrillator discharge, without discriminating between periprocedural

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