



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Percutaneous Alcohol Septal Ablation for Hypertrophic Obstructive Cardiomyopathy

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Cardiac Event Monitors
Implantable Cardioverter Defibrillator (ICD)

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Coverage Policy

CIGNA covers percutaneous alcohol septal ablation (ASA) for individuals with hypertrophic obstructive cardiomyopathy as medically necessary when BOTH of the following criteria are met:

- severe heart failure symptoms (New York Heart Association [NYHA] class III or IV) (see below Appendix I); with failure, contraindication, or intolerance to pharmacological therapy
- left ventricular (LV) outflow tract gradient ≥ 50 mm Hg at rest or after provocation (with physiological exercise)

CIGNA does not cover alcohol septal ablation (ASA) for any other indication because it is considered experimental, investigational or unproven.

General Background

Hypertrophic cardiomyopathy (HCM) is a genetic cardiovascular disease characterized by left ventricular hypertrophy, disorganization of cardiac myocytes and myofibrils, myocardial fibrosis, and small-vessel disease. Asymmetrical septal hypertrophy is the most common type of HCM in the West, accounting for 70–75% of cases. Other types of hypertrophic cardiomyopathy include basal septal hypertrophy (10–15%), concentric hypertrophy (5%), hypertrophy of the lateral wall (1–2%), and apical hypertrophy (<5%). The incidence of HCM is approximately one in 500 in the United States. Symptoms may include chest pain, palpitations, dyspnea, and syncope, although many patients are asymptomatic. The first clinical sign of the condition may be sudden

cardiac death, which may occur at any age, frequently during or following physical exertion. Approximately 25% of patients with HCM have a resting pressure gradient in the outflow tract of the left ventricle caused by systolic anterior motion of the mitral valve leaflets. It is clinically important to distinguish between the obstructive and non-obstructive forms of the disease. Diagnosis of HCM is generally established with two-dimensional echocardiography, and the degree of left ventricular obstruction is assessed with continuous wave Doppler echocardiography.

Treatment of hypertrophic obstructive cardiomyopathy (HOCM) is determined by symptom severity. Medical treatment is directed toward symptom relief and prevention of endocarditis, arrhythmias, and sudden death by reducing the left ventricular outflow pressure gradient. Pharmacological therapy may include beta-adrenergic blockers, calcium-channel antagonists, and diuretics. Dual chamber pacemaker implantation may also be considered in selected patient subgroups, although it is not a primary treatment for the disease. Surgery may be considered for patients with outflow tract gradients greater than 50 mm Hg, either at rest or with provocation, who have severe limiting symptoms refractory to medical therapy. The ventricular septal myectomy procedure, also known as the Morrow procedure, has become established as a standard therapeutic option for alleviation of outflow obstruction, and is the gold standard for adults and children with HOCM and severe drug-refractory symptoms. Septal myectomy has low operative mortality (1–3%) at centers having the most experience with this procedure, and has been associated with persistent, long-lasting improvement in disabling symptoms and exercise capacity (Maron, et al., 2003; McKenna and Elliott, 2007; Libby: Braunwald's Heart Disease, 2007).

Percutaneous alcohol septal ablation (PTASA), also referred to as percutaneous transluminal septal myocardial ablation (PTSMA) and transcatheter ablation of septal hypertrophy (TASH), is a catheter interventional procedure developed as a nonsurgical alternative to myectomy. Absolute alcohol is introduced into a target septal perforator branch of the left anterior descending coronary artery in order to produce a myocardial infarction in the proximal ventricular septum. The ablation mimics the hemodynamic results of myectomy, reducing the basal septal thickness and enlarging the left ventricular outflow tract, reducing mechanical impedance to left ventricular ejection. Although immediate rapid reduction of the resting outflow gradient may occur, more frequently a progressive decrease occurs after 6–12 months. Reported complications include complete heart block requiring pacemaker insertion, coronary dissection, and the need for mitral valve replacement. Alcohol septal ablation is contraindicated in patients with concomitant cardiac disease requiring surgery, and in patients with hypertrophic cardiomyopathy without outflow tract gradient.

Literature Review

Dwon et al. (2008) evaluated outcomes of ASA performed at the Cleveland Clinic between 1997 and 2000 in 55 high-risk patients with symptomatic HOCM. Surgical myectomy is considered the preferred treatment at this institution. The patients included in this study of ASA were considered at high risk for surgical myectomy due to age or comorbidities. Evaluation at baseline, three months, and one year included septal thickness, maximal LVOT gradient, Minnesota living with heart failure questionnaire score, and the presence of a permanent pacemaker. At three months, mean maximal LVOT gradient improved from 104 ± 35 mm Hg to 49 ± 28 mm Hg; septal thickness improved from 2.4 ± 0.4 cm to 1.8 ± 0.6 cm, and the Minnesota living with heart failure scores improved from 63 to 25 (all $p < 0.001$). No significant changes were seen at one year. Permanent pacemakers were implanted in 14 of 55 (25%) patients following ASA. No patients died at 48 hours, two died at one year, seven died at five years, and 13 died at ten years. Only age > 65 at the time of the procedure was a predictor of long-term mortality. The authors concluded that ASA is associated with symptomatic improvement and low short-term mortality, and is a viable option for HOCM patients at high risk for surgery.

Fernandes et al. (2008) evaluated the long-term outcome of ASA as treatment for symptomatic HOCM in a series of 619 patients treated between 1996 and 2006. A total of 92% of patients were available at follow-up in 2007. At a mean follow-up of 4.6 ± 2.5 years (range three months to 10.2 years) NYHA functional class decreased from 2.8 ± 0.6 to 1.2 ± 0.5 ; Canadian Cardiovascular Society angina score decreased from 2.1 ± 0.9 to 1.0 ± 0 ; and exercise time increased from 4.8 ± 3.3 to 8.2 ± 1.0 minutes (all $p < 0.001$). Resting and provoked LVOT gradient decreased progressively ($p < 0.001$) and remained low during follow-up. The septal thickness decreased from 2.0 ± 0.5 cm to 1.0 ± 0.1 cm ($p < 0.001$), and ejection fraction decreased from $68 \pm 9\%$ to $62 \pm 3\%$ ($p < 0.001$). Survival estimates were 97%, 92%, and 89% at one, five and eight years, respectively. The authors concluded that ASA results in sustained clinical and hemodynamic improvement.

Kuhn et al. (2007) reported on the impact of alcohol ablation on the survival of all patients with HOCM treated at a single center from 1995–2005. A total of 644 consecutive patients were divided into two groups. Group A was

comprised of the first 329 patients who were treated in a dose finding strategy with decreasing amounts of ethanol until December 2001. On average, Group A received between 2.9 ml and 0.93 ml of alcohol per patient. Group B consisted of the next 315 patients who received low alcohol doses (0.3–1.5ml per patient). The all-cause annual mortality was 4.3% for patients in Group A, and 2.1% in Group B. Following discharge, the annual cardiac mortality was 0.6% for Group A and 1.0% for Group B. Age was identified as an independent predictor of increased overall mortality ($p = 0.002$) and lower alcohol dosage and the absence of atrial fibrillation as independent predictors of reduced cardiac mortality ($p = 0.005$ and $P = 0.039$, respectively). The authors stated that his data suggests that with increasing procedural experience, including a reduction in the amount of ethanol used, in-hospital mortality has become very low and cardiac survival is high, although the risk of sudden death was not completely eliminated.

Ralph-Edwards et al. (2005) compared outcomes following isolated surgical myectomy ($n=60$) and alcohol ablation ($n=54$) in symptomatic adults treated at a single center between 1998 and 2003. Adjustments using a propensity score were used in the clinical and hemodynamic outcomes to accommodate for the differences in baseline patient characteristics and the lack of randomization. There were five late deaths in the ablation group and one late death after myectomy. Both procedures offered substantial clinical improvement for patients with HOCM, and there was no significant difference in post-intervention pacing, after adjustment for baseline variables. Significantly more patients achieved the defined optimal outcome (defined as survival, NYHA functional class I, no post-procedure pacemaker placement, and follow-up resting left ventricular outflow gradient of less than 20 mm Hg) after myectomy (73%) than after alcohol ablation (22%). The authors noted that the results from this study may not be generally applicable, as surgical myectomy is an established procedure at their facility, and ablation is a new, evolving technique.

Systematic Reviews/Meta-Analyses

Alam et al. (2009) conducted a meta-analysis of alcohol septal ablation vs. myectomy for hypertrophic obstructive cardiomyopathy (HOCM). Five non-randomized studies were included. Of 351 patients, 183 underwent alcohol septal ablation (ASA) and 168 underwent myomectomy. All patients were in NYHA class II-IV, and baseline left ventricular outflow tract (LVOT) gradient was comparable in both groups. After septal reduction therapy, resting LVOT gradient was < 20 mm Hg in both groups at follow-up. Patients who underwent myomectomy had lower LVOT gradient (18.2 ± 6.7 vs. 10.8 ± 6.3 mm Hg, $p<0.001$). Comparable improvements in NYHA class were seen in both groups at follow-up (1.5 ± 0.3 for ASA vs. 1.3 ± 0.2 for myomectomy, $p=0.2$). Permanent pacemaker implantation for complete heart block was required in a higher percentage of ASA patients (18.4 ± 7.9 vs. 3.3 ± 3.9 , $p=0.04$). There was no significant difference in hospital mortality between the two groups.

Zeng et al. (2006) conducted a meta-analysis to compare PTSMA to septal myectomy. The analysis included three nonrandomized comparative studies with a total of 177 patients; 86 were treated with PTSMA, and 91 were treated with myectomy. There were no significant differences in outcomes between the two groups in terms of decrease in interventricular septum thickness, increase in left ventricular end-diastolic dimension, and improvement in NYHA class. Improvement in left ventricular outflow tract gradient was greater in the in the PTSMA group (decrease from 76.0 to 15.7 mm Hg) than in the myectomy group (decrease from 74.7 to 9.4 mm Hg). The authors suggested the need for large, randomized controlled trials, including exercise test parameters and long- term prognosis, to compare these treatments.

Alam et al. (2006) conducted a systematic review of the literature published from 1996– 2005 evaluating outcomes and complications after ASA. Forty-two published studies, primarily uncontrolled case series, involving 2959 patients, were reviewed. Most The mean age at ablation was 53.5 years, and the mean follow-up was 12.7 months. At 12 months, there was a sustained decrease in resting and provoked left ventricular outflow tract (LVOT) gradient, a reduction in basal septal diameter, improved NYHA class and increased exercise capacity. The most common complication was complete heart block requiring permanent pacemaker implantation. Additional complications included ventricular fibrillation, LAD dissection, and pericardial effusion. According to the authors, the short- and intermediate-term follow-up has been promising, but the long-term follow-up is still not available. The authors stated that ASA is effective in reducing symptoms in the short- and intermediate-term follow-up. They recommend stringent criteria for patient selection as well as proper training to prevent adverse outcomes. The authors concluded by stating that randomized controlled trials comparing myectomy with ASA are necessary to assess the effectiveness of these treatments.

ECRI

An ECRI Institute Health Technology Assessment, Percutaneous Transcatheter Septal Myocardial Ablation for Hypertrophic Cardiomyopathy (ECRI, 2002), states that the available studies, consisting of two retrospective controlled studies comparing PTSMA and myectomy and seven retrospective uncontrolled case series, had relatively weak designs. The latter design cannot separate placebo effects from improvement due to an actual treatment effect. The retrospective comparative studies are vulnerable to selection bias that could make a treatment appear to be more effective than it actually is relative to the comparison treatment. The report concluded that PTSMA was associated with improvement of HOCM symptoms, and that results were comparable to surgical myectomy. The report states that better-designed trials are needed to allow definitive conclusions regarding the relative effectiveness of PTSMA and surgical myectomy.

National Institute for Clinical Excellence (NICE) (United Kingdom)

NICE guidance published in 2004 states that the current evidence on the safety and efficacy of nonsurgical reduction of the myocardial septum appears adequate to support the use of this procedure. NICE recommended the procedure only be performed in specialty units by clinicians who have had adequate training in the technique.

Professional Societies/Organizations

The American College of Cardiology (ACC) Committee for Practice Guidelines and the European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy states that proper selection of patients for alcohol septal ablation remains a crucial issue. All candidates considered for alcohol septal ablation should have severe heart failure symptoms (NYHA classes III or IV) refractory to all medications utilized in HCM as well as a subaortic gradient of 50 mm Hg or more measured with Doppler echocardiography, either under basal conditions and/or with physiologic provocative maneuvers during exercise. The document states that, while alcohol ablation represents an available option for HCM patients and a selective alternative to surgery, it is not regarded as the standard and primary therapeutic strategy for all severely symptomatic patients refractory to maximal medical management with marked obstruction to LV outflow. Septal myectomy remains the gold standard for this HCM patient subset (Maron et al., 2003).

Summary

Surgical septal myectomy is an established treatment strategy for patients with symptomatic hypertrophic obstructive cardiomyopathy refractory to pharmacological therapy. Percutaneous alcohol septal ablation was developed as a less invasive alternative to surgical myectomy. Although percutaneous alcohol septal ablation has not been evaluated in randomized controlled trials, the available evidence indicates that the procedure results in improvement in hypertrophic obstructive cardiomyopathy symptoms, with a progressive reduction in outflow gradient over 6–12 months, usually reaching levels comparable to surgical myectomy. Based on the available peer-reviewed literature and consensus documentation, percutaneous alcohol septal ablation appears to be a reasonable treatment option for carefully selected patients with hypertrophic obstructive cardiomyopathy and severe heart failure symptoms (New York Heart Association [NYHA] classes III and IV).

Appendix I

New York Heart Association Classification of Heart Failure

Class	Patient Symptoms	Limitation
Class I	Ordinary physical activity does not cause undue fatigue, dyspnea, palpitation	None
Class II	Ordinary physical activity causes fatigue, dyspnea, palpitation, or angina	Slight
Class III	Comfortable at rest; less than ordinary physical activity causes fatigue, dyspnea, palpitation, or angina	Moderate
Class IV	Symptoms at rest; any physical activity increases discomfort	Severe

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary when used to report percutaneous alcohol septal ablation (ASA) and medical necessity criteria outlined in this Coverage Policy are met:

CPT ^{®*} Codes	Description
93799 [†]	Unlisted cardiovascular service or procedure

ICD-9-CM Diagnosis Codes	Description
425.1	Hypertrophic obstructive cardiomyopathy

Experimental/Investigational/Unproven/Not Covered:

ICD-9-CM Diagnosis Codes	Description
	All other codes

*Current Procedural Terminology (CPT[®]) © 2010 American Medical Association: Chicago, IL.

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Policy History

<u>Pre-Merger Organizations</u>	<u>Last Review Date</u>	<u>Policy Number</u>	<u>Title</u>
CIGNA HealthCare	5/15/2008	0090	Percutaneous Alcohol Septal Ablation For Hypertrophic Obstructive Cardiomyopathy

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