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Clinical UM Guideline

Subject: Alcohol Septal Ablation for Treatment of Hypertrophic Cardiomyopathy
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Description

This document addresses alcohol septal ablation (ASA), a less invasive alternative to open surgical septal resection, for the treatment of hypertrophic cardiomyopathy (HCM) in adults. HCM is also referred to as hypertrophic obstructive cardiomyopathy (HOCM).

Clinical Indications

Medically Necessary:

Alcohol septal ablation is considered **medically necessary** as a treatment of hypertrophic cardiomyopathy (HCM) in individuals age 21 and older when **all** of the following criteria are met:

1. Severe heart failure symptoms (New York Heart Association [NYHA] class III or IV) or other exertional symptoms (such as syncope or near syncope) refractory to drug therapy; **and**
2. Left ventricular outflow tract (LVOT) gradient greater than or equal to 50 mm Hg at rest or with physiological provocation, including but not limited to: exercise, Valsalva maneuver or amyl nitrate.

Not Medically Necessary:

Alcohol septal ablation is considered **not medically necessary** when all of the above criteria are not met.

Coding

The following codes for treatments and procedures applicable to this guideline are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met:

CPT	
93583	Percutaneous transcatheter septal reduction therapy (eg, alcohol septal ablation) including temporary pacemaker insertion when performed
ICD-10 Procedure	
025M3ZZ	For the following procedure code **when specified as alcohol septal ablation**: Destruction of ventricular septum, percutaneous approach [*when specified as alcohol septal ablation*]
ICD-10 Diagnosis	
I42.1-I42.2	Hypertrophic cardiomyopathy

When services are Not Medically Necessary:
For the procedure and diagnosis codes listed above when criteria are not met.

Discussion/General Information

HCM is an inherited cardiovascular disease present in 1 in 500 of the general population (Maron, 2013) and is the most common genetic cardiac disease (Khouzam, 2014). One of the most characteristic abnormalities of this complex disease is a hypertrophied and nondilated left ventricle, which may impair diastolic filling. When the hypertrophy results in left ventricular outflow obstruction, the development of dyspnea, angina, syncope, or congestive heart failure may occur. Pharmacologic therapies include beta blockers or calcium-channel blockers to decrease the heart rate with a consequent prolongation in diastole and increased passive ventricular filling. If medical therapy is insufficient to control symptoms, strategies to reduce the outflow obstruction may be considered. Surgical resection focuses on removing a small amount of myocardium at the base of the septum (myectomy).

ASA for treatment of HCM has been considered as an alternative to open surgical septal resection in adults. The technique involves infusion of ethanol through an angioplasty catheter threaded into the septal perforator branches of the left anterior descending artery intended to infarct and subsequently thin the bulging septum. A key component of the procedure is the identification of the target vessels. A balloon catheter is introduced into the septal branches. The balloon is inflated and contrast injected into the balloon lumen to delineate the area supplied by the septal branch and to ensure that the balloon inflation would prevent spillage of the subsequent injection of alcohol into the left anterior descending artery.

Clinical evidence evaluating ASA indicates that in certain adults, the procedure may result in improvement of various signs and symptoms including NYHA classification, exercise time, LVOT gradient, and septal thickness as measured by echocardiography. There is a lack of randomized trials evaluating the procedure; however, case series, meta-analyses and practice guidelines are available.

Seggewiss and colleagues (1999) conducted a single-group study with a pre-post design to evaluate outcomes of individuals with symptomatic HCM who underwent treatment with ASA. A total of 114 individuals underwent ASA, and clinical and echocardiographic exams were performed at baseline, and at 3 months (n=87) and 1 year (n=33) post-procedure. LVOT gradient was reduced in 94% of individuals from a mean of 73.8 ± 36.5 to 18.6 ± 19.7 mm Hg at rest ($p<0.00001$). The NYHA classification also improved, with all individuals at baseline with a functional class of II to IV to all individuals with class I or II ($p<0.0001$) at follow-up. A total of 11 (9.6%) individuals required a permanent pacemaker due to trifascicular block, and 2 individuals (1.8%) died during the hospital stay. Kuhn

and colleagues (2000) reported on a case series of 215 ASA procedures in 187 individuals. The perioperative mortality rate was 2.3%. At a mean follow-up of 2.4 years, the NYHA classification had decreased from 3.0 to 1.6. Similar to the data reported by Seggewiss, there were significant improvements in cardiodynamic measures, including outflow gradient and septal thickness. Gietzen and colleagues (1999) reported on 62 individuals with HCM undergoing ASA, all of whom had substantial clinical improvement. The procedure-related early mortality was 4%, and a permanent pacemaker was required in 40% of the cases. Lakkis and colleagues (2000) reported on the 1-year follow-up of 50 individuals with HCM undergoing ASA. A total of 16% required permanent pacemaker implantation. There were 2 perioperative deaths (4%). Prior to the procedure, all individuals reported either NYHA Class III or IV symptoms compared to none at 1 year follow-up. Improvement in cardiodynamic assessments was consistent with the clinical improvements.

Fernandes and colleagues (2008) conducted a single-group study with a pre-post design to evaluate long-term outcomes of individuals who underwent ASA. A total of 629 subjects were consecutively enrolled from 1996 to 2007. Of the enrollees, 98.4% (n=619) underwent ASA with 92% having follow-up exams in 2007. During the procedure, ethanol (2.6 ± 1.0 ml) was injected into 1.3 ± 0.5 septal arteries. The median follow-up was 4.5 years (interquartile range [IQR], 2.75 to 6.36 years). During follow-up, the mean NYHA functional class decreased from 2.8 ± 0.6 to 1.2 ± 0.5 ($p<0.001$), the mean Canadian Cardiovascular Society (CCS) angina score decreased from 2.1 ± 0.9 to 1.0 ± 0 ($p<0.001$), and mean exercise time increased from 4.8 ± 3.3 to 8.2 ± 1.0 ($p<0.001$) minutes. At baseline, 503 individuals had an LVOT gradient at rest ≥ 30 mm Hg (mean 77 ± 31 mm Hg). The mean LVOT gradient at rest decreased at 3 months and 1 year after the procedure (26 ± 27 mm Hg [n=404] and 20 ± 24 mm Hg [n=258], respectively). The mean septal thickness decreased from 2.1 ± 0.5 cm to 1.0 ± 0.1 cm ($p<0.001$) at 3 months, and 1.5 ± 0.4 cm at 1 year. The mean ejection fraction decreased from 68 ± 9% to 65 ± 9 % ($p<0.001$) at 3 months and remained in the range of 60 to 65% throughout the follow-up period. Complications included death 1% (n=6), the need for a permanent pacemaker 8.2% (n=52), coronary dissection 1.3% (n=8), and worsening mitral regurgitation 0.3% (n=2). Kaplan-Meier estimates of survival at 1, 5, and 8 years were 97%, 92%, and 89%, respectively. The investigators concluded in this single-group study, the clinical and hemodynamic improvements after ASA were maintained throughout the follow-up period.

Nagueh and colleagues (2011) conducted a single-group study with a pre-post analysis to identify predictors of clinical outcomes of individuals who underwent ASA for the treatment of HOCM. A total of 874 individuals who underwent ASA were enrolled in a multicenter North American Registry. Most subjects (64%) had severe obstruction at rest, and 36% had provocable obstruction. Prior to ablation, 78% of the subjects had severe dyspnea (NYHA functional class III or IV) and 43% had severe angina (CCS angina class III or IV) with or without dyspnea. The mean follow-up duration was 776 ± 26 days. Significant improvement occurred after ablation; however, there were 81 deaths (9.3%). Kaplan-Meier estimates of survival at 1, 5, and 9 years were 97%, 86%, and 74%, respectively. Survival appeared better after ASA as compared to historical controls who did not undergo septal reduction therapy (Ommen, 2005). Baseline variables that predicted mortality after ablation included a lower baseline ejection fraction ($p=0.01$) and NYHA functional class ($p=0.02$). Procedural predictors included the number of septal arteries injected with ethanol (with more arteries injected associated with lower mortality; $p=0.007$), the volume of ethanol injected (with higher volume associated with lower mortality; $p<0.001$) and post-procedurally, a more effective ablation was associated with a lower likelihood of death, for example, smaller septal thickness after 3 months ($p=0.03$), greater symptomatic improvement (lower NYHA class; $p<0.001$), not taking beta-blockers ($p=0.002$) or verapamil ($p=0.049$) post ablation, and not having the need for repeat septal ablation procedures ($p<0.001$). The investigators stated that this study has a number of clinical implications: 1) ASA is an invasive procedure with the risk of death and significant morbidity; 2) care should be used when selecting individuals to undergo ASA; 3) ASA should be performed by experienced individuals; 4) trying to achieve the most successful hemodynamic response with the initial ablation procedure, if technically possible, rather than accepting high residual gradients and repeating the ablation at a later point in time; 5) due to the higher mortality in individuals who undergo a second ASA, consider myectomy rather than a repeat ASA.

Jensen and colleagues (2013) conducted a single-group study with a pre-post design to assess survival, effects on traditional risk factors (RFs), and the incidence of sudden cardiac death (SCD) following treatment with ASA. A total of 470 consecutive subjects (age 56 ± 14 years) with HCM (1996-2010) underwent clinically applied echo-contrast-guided ASA treatments. All-cause mortality, SCD, and RFs for SCD before and after ASA were evaluated. The mean follow-up period was 8.4 ± 4 years. The Kaplan-Meier estimate of 10-year survival after ASA was 88% compared with 84% in a matched (age and gender) background population from Statistics Denmark (2009; $p=0.06$). The 10-year survival free of SCD was 95% (annual SCD rate 0.5%). ASA decreased the prevalence of abnormal blood pressure response from 23% to 9% ($p<0.001$), syncope from 26% to 2% ($p<0.001$), non-sustained ventricular tachycardia (NSVT) from 23% to 17% ($p<0.05$) and maximal wall thickness ≥ 30 mm from 7% to 2% ($p<0.001$). The proportion of high-risk individuals (having 2 or more RFs) decreased from 25% (n=89) to 8% (n=23; $p<0.001$). The authors concluded that ASA was safe due to the significant reduction in the number of high-risk individuals and low incidence of SCD, and that a revised risk stratification routine for individuals with HCM and treated with ASA may be clinically useful.

Moss and colleagues (2014) conducted a single-group study with a pre-post design to evaluate LV function and clinical outcomes of 145 individuals who were diagnosed with HCM and underwent 167 ASA procedures from 2002 to 2011. Prior to the procedure, all individuals had a normal baseline left ventricular ejection fraction (LVEF) of more than 55%. Echocardiographic follow-up was available in 139 (96%) of the cases. Of those with echocardiographic follow-up performed post ASA, LVEF was preserved in 97.1% of cases over a mean follow-up time of 3.1 ± 2.3 years. Mild LV systolic dysfunction was observed (LVEF range 44% to 54%) in 4 cases. Mitral regurgitation severity improved in 67%. Resting LVOT gradient declined from a mean of 75 to 19 mm Hg ($p<0.001$), and provoked gradient declined from a mean of 101 to 33 mm Hg ($p<0.001$). NYHA class improved from a mean of 2.9 ± 0.4 to 1.3 ± 0.5 ($p<0.001$). A total of 16 deaths (11%) occurred, at least 3 of which were most likely due to cardiovascular causes. Kaplan-Meier estimates of survival at 1, 3 and 5 years post ASA were 96%, 90%, and 85%, respectively. Study limitations included lack of a control or comparison group. The authors concluded that their study suggests that “LV systolic function is preserved in most patients treated with ASA, and corresponding improvements in functional capacity and echocardiographic parameters were observed in the majority.”

Veselka and colleagues (2014a) conducted a single-group retrospective analysis to evaluate long-term outcomes of 75 individuals age 50 years or less who were highly symptomatic from HOCM and underwent ASA at three European centers. The primary endpoint was all-cause mortality. All individuals underwent clinical, electrocardiographic, and echocardiographic exams at baseline, 3 to 6 months post procedure and then yearly. Median duration of follow-up was 5.1 years (range, 0.1 to 15.4 years). A total of 5 individuals had an implantable cardioverter-defibrillator (ICD) implanted before ASA, and 7 individuals were implanted with ICDs during the study period. No individuals were lost to follow-up however, during the study period, 4 individuals (5%) died. In 2 of those individuals, the causes of death (sudden death and stroke) were at least partly attributed to HCM. The Kaplan-Meier estimates for survival free of all-cause mortality combined with the first appropriate ICD discharge at 1, 5, and 10 years were 96%, 91%, and 91%, respectively. The annual mortality combined with the first appropriate ICD discharge was 1.43% (95% confidence interval [CI], 0.52 to 3.10%). A total of 85% reported improvement of dyspnea and 93% reported improvement of angina. The authors concluded that these results suggest that individuals who are 50 years of age or less with highly symptomatic HOCM and undergo ASA are at minimal risk for all-cause death or appropriate ICD discharge in the long term.

Veselka and colleagues (2014b) conducted a single-group study with a pre-post design to evaluate outcomes of individuals who were diagnosed with HOCM, highly symptomatic, and underwent ASA. Data for this analysis was derived from the Euro-ASA registry. A total of 459 individuals (age 57 ± 13 years), who were diagnosed with HOCM and highly symptomatic, underwent ASA from 1999 to

2012. The primary endpoint was decrease in dyspnea by one or more NYHA functional class and the secondary endpoint was a decrease in pressure gradient by ≥ 50% or to ≤ 30 mm Hg. All individuals underwent clinical, electrocardiographic, and echocardiographic exams at baseline and 3 to 6 months after ASA. A total of 23 individuals were lost to follow-up and 3 individuals died. The mean follow-up was 113 ± 40 days. At follow-up, a total of 370 (85%) individuals had a 1 or more functional class reduction in their NYHA classification compared to baseline (p<0.01). Of the 63 individuals who did not report an improvement in dyspnea, 34 experienced an improvement in their CCS angina score or number of syncope events. The mean NYHA functional class and CCS angina score decreased from 2.8 ± 0.6 to 1.6 ± 0.6 and 1.7 ± 1.1 to 0.7 ± 0.7, respectively (p< 0.01 for both). The median outflow gradient decreased from a median of 88 mm Hg (IQR, 58 to 123 mm Hg) to 21 mm Hg (IQR, 11 to 41 mm Hg; p<0.01). A total of 29 individuals did not report any symptomatic improvement at follow-up. Compared to baseline, ASA also led to a reduction in basal septum thickness and left atrium diameter (p<0.01 for both). However, there was an increase in the median LV diameter (<0.01). The incidence of 3-month major adverse events (death, electrical cardioversion for tachyarrhythmias, resuscitation) and mortality was 2.8% and 0.7%, respectively. There were 43 individuals who underwent permanent pacemaker implantation due to complete heart block post-ASA. In this observational study, early outcomes suggest that individuals with highly symptomatic HOCM who underwent ASA had significant improvements in dyspnea, angina, and the number of syncope events.

Vriesendorp and colleagues (2014) conducted a multicenter cohort analysis to evaluate long-term outcomes (all-cause mortality and SCD) of individuals diagnosed with HOCM and treated with medical treatment only, ASA or myectomy. A total of 1065 individuals were diagnosed with HCM, and LVOT gradient was measured to identify those with HOCM, which was defined as having an LVOT gradient of ≥ 30 mm Hg, at rest or after provocation. Individuals whose LVOT gradient was < 30 mm Hg after provocation were considered to have non-obstructive HCM and used as a control group. Invasive therapy was indicated if the peak LVOT gradient was ≥ 50 mm Hg, ventricular septal thickness was ≥ 15 mm, and there was persistent NYHA functional class III or IV dyspnea or CCS class III or IV angina despite optimal medical therapy only. A total of 690 individuals had an LVOT gradient of ≥ 30 mm Hg and of those, 124 received medical treatment only, 316 underwent ASA, 250 underwent myectomy, and 349, with non-obstructive HCM, were controls. Individuals in the ASA group were older (58 ± 14 years) when compared to those in the myectomy and medically treated groups (52 ± 16 years; p<0.001 and 53 ± 15 years; p=0.001, respectively). At baseline, most (87%) of those in the medically treated group had NYHA class I or II symptoms, and a higher proportion of the individuals who underwent myectomy had ≥ 2 risk factors for SCD than those who underwent ASA (p=0.009). The mean follow-up period was 7.6 ± 5.3 years. There was no difference in 5- or 10-year survival between those in the medically treated group who had NYHA class I or II, those who underwent ASA or myectomy and the control group. Multivariate analysis was used to determine independent predictors of all-cause mortality and showed that those included age (p<0.001) and systolic dysfunction with LVEF < 50% (p=0.005). There were 76 individuals with SCD over 8003 patient-years (0.9% per year). Between the groups, the annual rates of SCD ranged from 0.76% to 1.26%. Independent predictors of SCD included surviving ventricular fibrillation or sustained ventricular tachycardia (Hazard ratio [HR], 6.0; 95% CI, 3.4 to 10.6; p<0.001), having ≥ 2 established risk factors (HR, 2.7; 95% CI, 1.6 to 4.4; p<0.001), having atrial fibrillation (HR, 1.7; 95% CI, 1.1 to 2.8; p=0.03), and when compared to myectomy, undergoing ASA (HR, 2.1; 95% CI, 1.0 to 4.4; p=0.04) and receiving medical treatment only (HR, 2.3; 95% CI, 1.1 to 5.1; p=0.04). The authors concluded that this multicenter observational study showed that mortality rates are similar between those who underwent ASA or myectomy, were medically treated and had NYHA class I or II compared to those with non-obstructive HCM, and that the long-term risk for SCD was lower after myectomy compared to ASA or after receiving only medical treatment.

Veselka and colleagues (2016) conducted a single-group study with a pre-post design to evaluate outcomes of individuals who were diagnosed with HOCM, highly symptomatic, and underwent ASA. Data for this analysis was derived from the Euro-ASA registry. The ASA procedures were performed at 10 tertiary centers from seven European countries and by experienced interventional cardiologists. There were differences in post-procedural follow-up among participating centers but typically follow-up occurred at 3 to 6 months post ASA and then yearly thereafter. Study endpoints included survival and clinical outcomes of individuals treated with ASA, predictors of mortality events and clinical outcomes, and the relationships between the alcohol dose received and the improvement of LVOT gradient as well as the occurrence of complete heart block. A total of 1275 individuals (aged 58 ± 14 years, 49% females) who were highly symptomatic from HOCM and with no mitral valve disease or other indication for cardiac surgery were included in the analysis. These individuals underwent treatment from 1996 to 2005. The median follow-up period was 5.7 years. There were 13 deaths (1%) within the first month of ASA (4 cases of heart failure, 3 cases of pulmonary embolism, 2 cases of cardiac tamponade, and 1 case each of sepsis, stroke, carcinoma, and sudden cardiac death). A total of 171 (13%) deaths occurred overall during 7057 patient-years of follow-up, which was a post-ASA all-cause mortality rate of 2.42 (95% CI 2.07 to 2.82) deaths per 100 patient-years. Kaplan-Meier estimates of survival at 1, 5 and 10 years post ASA were 98%, 89% and 77%, respectively. Multivariate analysis was applied to determine independent predictors of all-cause mortality, and those included higher age at ASA (p<0.001), septum thickness prior to ASA (p<0.001), NYHA class before ASA (p=0.047) and LVOT gradient at last clinical exam (p=0.048). The alcohol dose during ASA procedures ranged from 0.4 to 11 mL, with a median dose of 2.0 mL, and 90% of the individuals were treated with 1 to 3 mL. Multivariate analysis was also used to evaluate the relationship between alcohol dose and the relative pressure gradient. Independent predictors of the delta pressure gradient included the volume of injected alcohol (p<0.001) and septum thickness and NYHA class at the last clinical exam (p<0.001 and p=0.005, respectively). A larger volume of alcohol was more effective in decreasing LV outflow tract gradient however, it was also associated with a higher occurrence of complete heart block (odds ratio [OR], 1.19; 95% CI, 1.05 to 1.35; p=0.006). In this observational study, individuals with HCM and treated with ASA had relief of symptoms and a reduction of LVOT obstruction, and while higher doses of alcohol are slightly more effective in reducing LV obstruction it resulted in a higher incidence of peri-procedural complete heart block. The authors concluded that this observational study showed that in carefully selected individuals who are highly symptomatic due to HOCM, ASA has low rates of peri-procedural and long-term mortality, and that optimal therapy should be focused on the elimination of LVOT gradient.

Veselka and colleagues (2017) conducted a single-group study with a pre-post design to evaluate outcomes of individuals who were diagnosed with HOCM, mildly symptomatic, and underwent ASA. Data for this analysis was derived from the Euro-ASA registry, and individuals were treated from January 2006 to May 2016. A total of 1427 consecutive individuals were treated with ASA for HOCM, and a subset of 161 individuals (53 ± 13 years; 73% male) with baseline NYHA class II dyspnea and LVOT obstruction ≥ 50 mm Hg at rest or after provocation were included in the analysis. Study endpoints included survival post-ASA (compared to a gender- and age-matched general population; Veselka, 2014c), symptomatic improvement post-ASA, progression of heart failure symptoms post-ASA, and predictors of an adverse clinical outcome. The median duration of follow-up was 4.8 years (IQR, 1.7 to 8.5 years). After ASA, the 30-day mortality rate was 0.6%, and the annual all-cause mortality rate was 1.7%, which did not differ from the expected rate in the general population after adjusting for age and gender (p=0.62). There were improvements in NYHA class, LV gradient at rest, and basal septum thickness (2.0 ± 0 to 1.3 ± 0.1; 63.3 ± 31.7 to 14.6 ± 19.0 mm Hg; 20.6 ± 4.3 to 15.7 ± 4.4 mm, respectively; p<0.01 for all). LVEF decreased from 71 ± 9 to 68 ± 8 (p=0.02). LV diameter increased from 43.8 ± 6.7 to 46 ± 5.8 mm (p<0.01). Kaplan-Meier estimates for survival free of all-cause mortality at 1, 5, and 10 years were 97%, 94% and 87%, respectively. Estimates for survival free of all-cause mortality combined with the first appropriate ICD discharge or resuscitation at 1, 5, and 10 years were 97%, 91% and 87%, respectively. Multivariate analysis was used to identify independent predictors of all-cause mortality. Those included age at ASA and absence of improvement in NYHA at last clinical exam (p=0.04 for each). The investigators concluded that this observational study showed that individuals with mildly symptomatic HOCM and severe LVOT obstruction who undergo ASA have a long-term prognosis that is comparable to an age- and gender-matched general population.

An and colleagues (2017) conducted a cohort analysis to evaluate complications and long-term outcomes of individuals who were diagnosed with HOCM and underwent ASA, and compared their prognosis to individuals with nonobstructive hypertrophic cardiomyopathy (NOHCM; control group). A total of 530 individuals were consecutively enrolled, with 233 individuals (43.96%) in the ASA group, and 297 individuals (59.04%) in the control group. The ASA group were older than the control group (48.7 ± 9.8 vs. 46.2 ± 13.6 years; p=0.018) and had a higher proportion of individuals with NYHA functional class of III/IV, CCS class III/IV and syncope/presyncope events (78 vs. 3.7%, 33.9 vs. 3.7% and 48.5 vs. 9.4%, respectively; p<0.001 for all). The ASA group had a lower proportion of individuals with atrial fibrillation (8.6 vs. 16.8%; p=0.009) and there was no difference between the groups in the proportion of individuals with a prior stroke or transient ischemic attack, diabetes, hypertension, or coronary artery disease (CAD). The follow-up duration for the ASA and control groups were similar (6.03 ± 3.25 and 6.07 ± 4.47 years, respectively; p=0.911). In the ASA group, the peri-procedural mortality rate was 0.89% (n=2). Multivariate analysis showed that alcohol volume and age ≤ 40 years were associated with higher risk for procedural sustained ventricular tachycardia or ventricular fibrillation (relative risk [RR], 1.44; 95% CI, 1.03 to 2.03; p=0.034 and RR, 4.63; 95% CI, 1.07 to 20.0; p=0.040, respectively). Between the groups, there was no difference in the long-term prognosis, which included survival free from all-cause mortality (p=0.764), cardiovascular mortality (p=0.611) or SCD (p=0.778). The investigators concluded that their analysis showed that the long-term prognosis of individuals who undergo ASA is adequate, individuals aged 40 years or less have a higher incidence of periprocedural ventricular arrhythmias, and mortality (all-cause, cardiovascular and SCD) rates are similar to individuals with NOHCM.

Nguyen and colleagues (2019) conducted a single-center cohort analysis to compare early and late outcomes of individuals who underwent septal myectomy (n=1284) vs. ASA (n=211). Outcomes included procedure-related morbidity and mortality, gradient relief, freedom from reintervention and functional improvement. Propensity score (PS) matching (2:1) was used to minimize differences between the cohorts. A multivariable logistic regression model estimated the effects of 15 covariates: age at intervention, gender, procedure year, NYHA class, presence of select comorbid conditions (chronic lung disease, renal failure, diabetes, hypertension, CAD), history of cerebrovascular accident, use of a beta blocker or calcium channel blocker, previous percutaneous coronary intervention or coronary bypass graft surgery, and LVOT gradient. The PS analysis matched 334 individuals who underwent myectomy to 167 individuals who underwent ASA, and after matching there were no differences between the groups for the 15 baseline covariates. There were no in-hospital deaths after septal myectomy or ASA. Between the groups, there were no differences in nonfatal complications (tamponade, sustained ventricular tachycardia/cardiac arrest, reoperation, or cerebrovascular accident), need for an implantable cardioverter defibrillators or survival. Permanent pacemaker insertion was significantly lower in the myectomy group (3.9 vs 17.4%, p<0.001). Reintervention for LVOT obstruction was more likely to occur in individuals who underwent ASA compared to myectomy (HR, 33.3; 95% CI, 4.4 to 250.6; p<0.001). In this observational study, which retrospectively evaluated data from individuals who underwent myectomy or ASA, there was no difference in survival but freedom from reintervention and late reduction of LVOT gradient were better in those who underwent myectomy. However, PS analysis is dependent on the appropriateness of the covariate selection and is unlikely to account for all possible confounders.

Studies have shown that gender and race/ethnicity disparities exist in the diagnosis and treatment of HCM. Butzner and colleagues (2022) evaluated 9306 individuals (males, 60.5%) with HCM and reported that females were more likely to have an echocardiogram (21.9 vs 20.1%, p=0.039) and less likely to undergo cardiac stress testing (6.8 vs 8.5%, p=0.004) compared to males. A lower proportion of females were prescribed beta-blockers compared to males (42.7 vs. 45.2%; p=0.017) while there was no difference in the use of calcium channel blockers or rates of ASA or myectomy. Fewer females had atrial fibrillation (6.7 vs. 9.9%; p<0.001), ventricular tachycardia/fibrillation (6.1 vs. 8.1%; p<0.001) and an implantable cardioverter-defibrillator (1.7 vs. 2.6%; p=0.005) compared to males. The authors concluded that their results may help providers in the treatment of females with obstructive HCM, and that future studies are needed to understand these potential disparities.

Eberly and colleagues (2020) evaluated outcomes from 2467 individuals who were diagnosed with HCM and self-reported as Black (n=205) or White (n=2262). Two composite outcomes were defined: 1) ventricular arrhythmic composite (first occurrence of sudden cardiac death, resuscitated cardiac arrest, or appropriate implantable ICD therapy or firing (nonantitachycardia pacing); and 2) overall composite (first occurrence of any component of the ventricular arrhythmic composite end point, cardiac transplant or left ventricular assist device implantation, NYHA class III or IV heart failure, atrial fibrillation, stroke, or all-cause mortality. Compared to White individuals, Black individuals were younger at diagnosis (p<0.001), had a higher prevalence of NYHA functional class of III or IV at presentation (p=0.001), lower rates of genetic testing (p=0.03), and among those who did receive genetic testing, less likely to have sarcomeric mutations (p=0.006). Invasive septal reduction therapies were performed less frequently in Black compared to White individuals (30 vs. 521 [14.6 vs. 23.0%]; p=0.007). In addition, a higher proportion of Black individuals underwent myectomy and a lower proportion underwent ASA compared to White individuals (93 vs. 86% and 6.7 vs. 11.3%, respectively; p-values not reported). Between the groups, there were no differences in the rates of stroke, ventricular arrhythmias, all-cause mortality, or the overall composite outcome. The authors concluded that their results suggest that there are racial inequities in healthcare access and delivery, and that an increase in minority group representation in healthcare studies is needed.

Patlolla and colleagues (2023) conducted a cross-sectional study to investigate whether racial and ethnic disparities exist among individuals who were hospitalized with HCM and underwent septal reduction therapy (SRT). Data for this study was derived from the Nationwide Inpatient Sample (NIS) from the Healthcare Cost and Utilization Project (HCUP) from January 2012 through December 2019. Adults (aged ≥ 18 years) with a primary diagnosis of obstructive HCM and had race and ethnicity information available were identified. A total of 18,895 individuals were admitted with obstructive HCM, and most were classified as White (n=13,885) followed by Black (n=2685), Hispanic (n=1235) and Other, which included Asian or Pacific Islander, Native American, and all Others (n=1090). Of those, a total of 7255 (38.4%) underwent SRT. Septal myectomy was performed on 4930 individuals, with the largest proportion classified as White (68.7%) followed by Black (7.6%), Hispanic (4.8%) and Other (4.3%). ASA was performed on 2325 individuals, with the largest proportion classified as White (80.6%) followed by Black (8.0%), Other (6.2%) and Hispanic (5.2%). A multivariable hierarchical logistic regression analysis was used to adjust for age, sex, primary payer status, median household income quartile, hospital characteristics, comorbidity index score, concomitant cardiac procedures, ventricular arrhythmias, and year of admission. The adjusted analysis showed that Black vs. White individuals were less likely to receive SRT (OR, 0.65; 95% CI, 0.57 to 0.73; p<0.001). Hispanic vs. White individuals were also less likely to receive SRT (OR, 0.78; 95% CI, 0.66 to 0.92; p=0.003). An adjusted subgroup analysis showed that use of septal myectomy was lower in the Black, Hispanic and Other groups compared to the White group (p<0.001, p=0.01, and p=0.003, respectively) however, there was no difference in the use of ASA between the groups. Among those undergoing SRT, in-hospital mortality was higher for the Hispanic and Other groups compared to the White group (p<0.001), while comparable to the Black group. The authors concluded that individuals who were hospitalized with obstructive HCM and classified as Black or Hispanic were less likely to receive SRT and those who were classified as Hispanic or Other had higher in-hospital mortality and complication rates. Additional research is needed to clarify the reasons for these disparities.

Other Considerations

Gersh and colleagues (2011) of the American College of Cardiology Foundation/American Heart Association Task Force on Practice guidelines issued a guideline for the diagnosis and treatment of HCM which includes the following invasive therapy recommendations:

CLASS I

1. Septal reduction therapy should be performed only by experienced operators in the context of a comprehensive HCM

clinical program and only for the treatment of eligible patients with severe drug-refractory symptoms and LVOT obstruction.† (Level of Evidence: C)
*Experienced operators are defined as an individual operator with a cumulative case volume of at least 20 procedures or an individual operator who is working in a dedicated HCM program with a cumulative total of at least 50 procedures.
†Eligible patients are defined by all of the following:

a. Clinical: Severe dyspnea or chest pain (usually NYHA functional classes III or IV) or occasionally other exertional symptoms (such as syncope or near syncope) that interfere with everyday activity or quality of life despite optimal medical therapy.
b. Hemodynamic: Dynamic LVOT gradient at rest or with physiologic provocation 50 mm Hg associated with septal hypertrophy and SAM of the mitral valve.
c. Anatomic: Targeted anterior septal thickness sufficient to perform the procedure safely and effectively in the judgment of the individual operator.

CLASS IIa

1. Consultation with centers experienced in performing both surgical septal myectomy and alcohol septal ablation is reasonable when discussing treatment options for eligible patients with HCM with severe drug-refractory symptoms and LVOT obstruction. (Level of Evidence: C)
2. Surgical septal myectomy, when performed in experienced centers, can be beneficial and is the first consideration for the majority of eligible patients with HCM with severe drug-refractory symptoms and LVOT obstruction. (Level of Evidence: B)
3. Surgical septal myectomy, when performed at experienced centers, can be beneficial in symptomatic children with HCM and severe resting obstruction (>50 mm Hg) for whom standard medical therapy has failed. (Level of Evidence: C)
4. When surgery is contraindicated or the risk is considered unacceptable because of serious comorbidities or advanced age, alcohol septal ablation, when performed in experienced centers, can be beneficial in eligible adult patients with HCM with LVOT obstruction and severe drug-refractory symptoms (usually NYHA functional classes III or IV). (Level of Evidence: B)

CLASS IIb

1. Alcohol septal ablation, when performed in experienced centers, may be considered as an alternative to surgical myectomy for eligible adult patients with HCM with severe drug-refractory symptoms and LVOT obstruction when, after a balanced and thorough discussion, the patient expresses a preference for septal ablation. (Level of Evidence: B)
2. The effectiveness of alcohol septal ablation is uncertain in patients with HCM with marked (i.e., >30 mm) septal hypertrophy, and therefore the procedure is generally discouraged in such patients. (Level of Evidence: C)

CLASS III: HARM

1. Septal reduction therapy should not be done for adult patients with HCM who are asymptomatic with normal exercise tolerance or whose symptoms are controlled or minimized on optimal medical therapy. (Level of Evidence: C)
2. Septal reduction therapy should not be done unless performed as part of a program dedicated to the longitudinal and multidisciplinary care of patients with HCM. (Level of Evidence: C)
3. Mitral valve replacement for relief of LVOT obstruction should not be performed in patients with HCM in whom septal reduction therapy is an option. (Level of Evidence: C)
4. Alcohol septal ablation should not be done in patients with HCM with concomitant disease that independently warrants surgical correction (e.g., coronary artery bypass grafting for CAD, mitral valve repair for ruptured chordae) in whom surgical myectomy can be performed as part of the operation. (Level of Evidence: C)
5. Alcohol septal ablation should not be done in patients with HCM who are less than 21 years of age and is discouraged in adults less than 40 years of age if myectomy is a viable option. (Level of evidence: C)

In 2020, the American Heart Association (AHA)/American College of Cardiology (ACC) issued an updated “guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy” (Ommen, 2020) which includes the following invasive treatment recommendations of symptomatic obstructive HCM:

CLASS I

1. In patients with obstructive HCM who remain severely symptomatic despite guideline-directed management and therapy (GDMT), *SRT in eligible patients*,* performed at experienced centers,† is recommended for relieving LVOT obstruction. (*Level of Evidence: B*)
2. In adult patients with obstructive HCM who remain severely symptomatic, despite GDMT and in whom surgery is contraindicated or the risk is considered unacceptable because of serious comorbidities or adverse age, *alcohol septal ablation in eligible patients*,* performed at experienced centers,† is recommended. (*Level of Evidence: C*)

* *Eligible patients are defined by all of the following*:

a. Clinical: Severe dyspnea or chest pain (usually NYHA functional classes III or IV) or occasionally other exertional symptoms (such as syncope or near syncope) that interfere with everyday activity or quality of life despite optimal medical therapy.
b. Hemodynamic: Dynamic LVOT gradient at rest or with physiologic provocation 50 mm Hg associated with septal hypertrophy and SAM of the mitral valve.
c. Anatomic: Targeted anterior septal thickness sufficient to perform the procedure safely and effectively in the judgment of the individual operator.
† Experienced operators are defined as an individual operator with a cumulative case volume of at least 20 procedures or an individual operator who is working in a dedicated HCM program with a cumulative total of at least 50 procedures.

CLASS IIb

1. For severely symptomatic patients with obstructive HCM, SRT in eligible patients,* performed at experienced centers†, may be considered as an alternative to escalation of medical therapy after shared decision-making including risks and benefits of all treatment options. (Level of Evidence: C)
2. For symptomatic patients with obstructive HCM in whom SRT is an option, mitral valve replacement should not be performed for the sole purpose of relief of LVOT obstruction. (Level of evidence: B)

CLASS III: HARM

1. For patients with HCM who are asymptomatic and have normal exercise capacity, SRT is not recommended. (Level of Evidence: C)
2. For symptomatic patients with obstructive HCM in whom SRT is an option, mitral valve replacement should not be performed for the sole purpose of relief of LVOT output. (Level of evidence: B)

Levels of Evidence and Classification of Recommendations:

Levels of evidence:
Level A: Multiple populations evaluated. Data derived from multiple randomized clinical trials or meta-analyses.
Level B: Limited populations evaluated. Data derived from a single randomized trial or nonrandomized studies.
Level C: Very limited populations evaluated. Only consensus opinion of experts, case studies, or standard of care.

Classification of Recommendations:
CLASS I: Procedure/Treatment SHOULD be performed/administered.
CLASS IIa: Additional studies with focused objectives needed. IT IS REASONABLE to perform procedure/administer treatment.
CLASS IIb: Additional studies with broad objectives needed; additional registry data would be helpful. Procedure/Treatment MAY BE CONSIDERED.
CLASS III: No benefit or may cause harm.

In response to these guidelines, Liebregts and colleagues (2017) evaluated if ASA is safe and effective for younger individuals compared to older individuals through a multicenter observational cohort study. Individuals were divided into three groups: young (less than or equal to 50 years, n=369), middle-age (51-64 years, n=423), and older (greater than or equal to 65, n=405). The primary endpoints, all-cause mortality rates and adverse arrhythmic event rates, were similar in all groups at about 1% (p=0.90). The evaluators concluded that the guidelines should expand ASA indications to younger individuals.

In 2014, Elliott and colleagues of the European Society of Cardiology (ESC) issued a guideline on the diagnosis and management of hypertrophic cardiomyopathy. The following information for ASA is included:

> In experienced centres, selective injection of alcohol into a septal perforator artery (or sometimes other branches of the left anterior descending coronary artery) to create a localized septal scar has outcomes similar to surgery in terms of gradient reduction, symptom improvement and exercise capacity. The main non-fatal complication is AV block in 7–20% of patients and the procedural mortality is similar to isolated myectomy.
>
> Due to the variability of the septal blood supply, myocardial contrast echocardiography is essential prior to alcohol injection. If the contrast agent cannot be localized exclusively to the basal septum at and adjacent to the point of mitral-septal contact, the procedure should be abandoned.
>
> Injection of large volumes of alcohol in multiple septal branches—with the aim of gradient reduction in the catheter laboratory—is not recommended, as it is associated with a high risk of complications and arrhythmic events.

Conclusion

In summary, data suggests that ASA for the treatment of HCM is associated with symptomatic and cardiodynamic improvement in adults under specific circumstances. Risks associated with the procedure include complete heart block requiring implantation of a permanent pacemaker, as well as an increased risk of sustained ventricular arrhythmias.

Definitions

Canadian Cardiovascular Society Score: This organization defines anginal classes as follows:

- Class I - Ordinary physical activity does not cause angina;
- Class II - Slight limitation of ordinary activity;
- Class III - Marked limitation of ordinary physical activity;
- Class IV - Inability to carry on physical activity without discomfort.

Left ventricular outflow tract (LVOT) gradient: A measurement often used to evaluate the severity of HCM, the presence or absence of LVOT obstruction, and the efficacy of treatment.

New York Heart Association (NYHA) functional class: A four-tier system that categorizes based on subjective impression of the degree of functional compromise. The four NYHA functional classes are as follows:

- Class I - Individuals with cardiac disease but without resulting limitation of physical activity; ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain; symptoms only occur on severe exertion;
- Class II - Individuals with cardiac disease resulting in slight limitation of physical activity; they are comfortable at rest; ordinary physical activity, (e.g., moderate physical exertion, such as carrying shopping bags up several flights of stairs) results in fatigue, palpitation, dyspnea, or anginal pain;
- Class III - Individuals with cardiac disease resulting in marked limitation of physical activity; they are comfortable at rest; less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain;
- Class IV - Individuals with cardiac disease resulting in inability to carry on any physical activity without discomfort; symptoms of heart failure or the anginal syndrome may be present even at rest; if any physical activity is undertaken, discomfort is increased.

Septal myectomy: A surgical procedure performed to reduce the muscle thickening that occurs in individuals with HCM.

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Index

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

History

Status	Date	Action
Reviewed	05/11/2023	Medical Policy & Technology Assessment (MPTAC) review. Updated Discussion/General Information and References sections.
Revised	05/12/2022	MPTAC review. Clarified clinical indication section changing adults to “individuals” in criteria. Updated Discussion and References sections.
Reviewed	05/13/2021	MPTAC review. Updated Discussion and References sections. Reformatted Coding section.
Reviewed	05/14/2020	MPTAC review.

New	06/06/2019	MPTAC review. Initial document development. Moved content of SURG.00133 Alcohol Septal Ablation for Treatment of Hypertrophic Cardiomyopathy to new clinical utilization management guideline document with the same title.
