Alcohol septal ablation for obstructive hypertrophic cardiomyopathy

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Chapter 11

Summary:

Chapter 1 first described the aetiology and pathophysiology of obstructive hypertrophic cardiomyopathy. Next, a description was given on the extensive and ongoing debate of the proper treatment of this patient group. This chapter also described the two main invasive treatment options, ASA and myectomy, their history in terms of associated complications and their improvements over time. Finally, the outline of the thesis was given. In short, the aim was to investigate and compare the two treatment options in terms of clinical outcome, predictors of clinical outcome and complication rates, and to identify possible means of improvement of ASA.

Chapter 2 described the background of HCM and the options for treatment. HCM is characterised by idiopathic left ventricular hypertrophy and estimated to have an incidence of 1:500 in the general population. It is inherited in an autosomal dominant fashion, with mutations in genes which encode for the sarcomere. Microscopy demonstrates hypertrophy and disarray of myocytes and interstitial and perivascular fibrosis can also be found. Systolic anterior motion of the anterior mitral valve leaflet with accompanying gradient obstruction in the left ventricular outflow tract can occur in 70% of patients with HCM. The ECG is abnormal in 80% of HCM patients and diagnosis is usually made by echocardiography, if not on cardiovascular magnetic resonance imaging. Symptoms of dyspnoea, angina, vertigo or syncope can occur in both obstructive and non-obstructive HCM patients. The clinical course of HCM patients is mostly favourable, with an annual mortality rate of 1%/year. However, in a high-risk population, the mortality rate can be higher than 5%/year. As sudden cardiac death can occur with no preceding symptoms, a careful risk assessment is necessary. Patients with an increased risk of sudden death can undergo ICD implantation.

In non-obstructive HCM patients, symptoms of reduced exercise tolerance can occur due to diastolic dysfunction and ischaemia. In these patients, medical treatment with beta blockers or verapamil usually does not improve – and may even worsen – heart failure symptoms due to negative inotropic effects. In contrast, for patients with symptoms due to obstruction of flow, beta blockers, verapamil and dysopiramide are treatment options as a first line. For patients in whom medical treatment has failed, invasive treatment of the obstruction can be undertaken using either surgical myectomy or – for those with relative contra-indications for myectomy – ASA.

In Chapters 3.1 and 3.2, the relationship between outcome after ASA and septal coronary anatomy was investigated. In Chapter 3.1, a case report illustrated the dependence of the operator on suitable septal anatomy. In cases where the operator was challenged with less favourable anatomy, the first result was inadequate; to achieve a successful outcome a second septal branch that was more proximal and more difficult to approach needed to be ablated. This illustrates the importance of coronary septal anatomy and infarct location for the outcome of the procedure.

In Chapter 3.2, predictors of an unsuccessful outcome after ASA were investigated, with a focus on septal anatomy. The definition of a successful outcome was the combination of a resting gradient < 30 mmHg, a provoked gradient < 50 mmHg and an improved NYHA class at follow-up. Coronary angiograms were evaluated for the presence of a septal branch that was more proximal than the ablated septal branch. Also the distance from the origin of the LAD to the origin of the ablated septal branch was measured. Univariate predictors for unsuccessful outcome after ASA were baseline gradient, distance to the ablated branch, and the presence of a non-ablated septal branch more proximal than the ablated branch. In the multivariate analysis, the combination of a non-ablated proximal septal branch with a more distal location of the ablated septal branch (>20 mm) was associated with an unsuccessful outcome. This confirms the importance of ablating the most proximal septal branch if the next septal branch is too distal. By applying this strategy, the infarction is more likely to encompass the entire basal part of the septum, leading to a wider left ventricular outflow tract (LVOT) and abolition of SAM and obstruction in the LVOT. These findings can be used periprocedurally in conjunction with MCE. And when anatomy is not suitable, patients may be referred for surgical myectomy instead.

Chapter 4 used CMR studies to investigate the effects of infarct location and infarct size on outcome after ASA in 47 patients with obstructive HCM. Infarct location was divided into "basal infarction" and "distal infarction". Infarct size was divided into small and large infarctions based on an optimal cut-off value for the distance from the basal septum to the beginning of the infarction. A more basal infarct location was found to be associated with a better outcome after ASA; and at long-term follow-up, patients with a basal infarct location also had lower gradients than those with a distal infarction. The reason for a more distal location of the infarction could be attributed to coronary septal anatomy. In contrast, a larger infarct size was not associated with lower gradients at follow-up. In the future, the best

strategy therefore seems to be to try and inflict a small basal infarction, which will maximise gradient abolition without risking possible complications seen for larger infarctions.

In Chapter 5, the relationship between alcohol dosage and infarct size, and cardiac death after ASA was investigated. The main finding was that alcohol dosage could not predict either ventricular arrhythmia or cardiac death. However, an association was found between infarct size and cardiac death. As it turned out, baseline septal thickness and larger septal branches were associated with infarct size, whereas alcohol dosage was not. Despite the lack of an association between alcohol dosage and cardiac death, a larger alcohol dosage was not associated with better gradient abolition, and thus it seems sensible to keep infarct size small and total alcohol dosage low.

In Chapter 6.1, in a single-centre study, a group of patients was investigated for periprocedural complications, symptoms of heart failure and long-term survival after ASA or myectomy. The rate of periprocedural complications after ASA was lower than that after myectomy and median in-hospital stay was shorter. The longer in-hospital stay and the higher rate of complications seen in myectomy are probably a reflection of the fact that this surgical procedure is more invasive than ASA. Survival, annual rate of cardiac death, symptomatic status at long-term follow-up, and rate of re-hospitalisation for heart failure were comparable between the two groups. However, the lower complication rate after ASA was offset by higher gradients after the procedure.

In Chapter 6.2, an editorial comment by Geske JB and Gersh BJ is given on the findings of Chapter 6.1, commenting on the fact that operative mortality, ischaemic stroke, need for re-thoracotomy due to bleeding and the need for PM implantation were relatively high compared with results from other high-volume centres (e.g. Cleveland Clinics and Mayo Clinic). The main probable reason as suggested by the authors is the difference in the surgeon's level of experience.

In Chapter 7.1, ASA and myectomy were compared in a multi-centre study. A control group consisting of patients with non-obstructive HCM was used for comparison. The annual rate of "cardiac death" was slightly higher after ASA than after myectomy and was mainly due to appropriate ICD shocks. However, overall survival was good and comparable after both ASA and myectomy. Both the reintervention rate and the gradient at follow-up were higher after ASA than after myectomy.

In Chapter 7.2, an editorial comment by Maron BJ and Nishimura RA is given on the findings of Chapter 7.1. The authors state that the American guidelines unanimously judge septal myectomy to be the primary treatment option for most patients with HCM. ASA is regarded as an alternative to myectomy only for patients with a very high perioperative risk or for patients of advanced age. They consider the two-fold increase in risk of sudden death after ASA to be an indicator of increased arrhythmogenicity due to the infarct induction with alcohol. They believe this to be an important reason why surgical myectomy should remain the primary treatment option.

In Chapter 8, the outcome after ASA was compared between a younger population (average 43 ± 8 years) and an older population (average 64 ± 6 years) and compared with age-matched control groups of pharmacologically treated HCM patients. The survival rate after ASA was similar in the two age groups and also similar to the respective control groups. Reduction of the gradient and post-procedural NYHA class after ASA were comparable between the young and older age groups. Regarding periprocedural complications, more PM implantations and a higher frequency of AV block were found in the older population.

Chapter 9 described the outcome after ASA of patients included in the European ASA registry, which included 1275 patients from ten centres in seven different countries. Perioperative mortality was 1% and survival rates after ASA were 98% at 1 year, 94% at 3 years, 89% at 5 years and 77% at 10 years. A small but significant association was found between residual obstruction and worse functional status. This illustrates the importance of completely eliminating the LVOT gradient.

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Curriculum Vitae

Robbert Steggerda is in 1974 geboren in Utrecht en opgegroeid in Echt, waar hij zijn vwo diploma in 1992. Hierna heeft hij in Antwerpen geneeskunde gestudeerd van 1992 tot 1997. Van 1997 tot 2001 heeft hij zijn opleiding geneeskunde afgerond aan de Vrije Universiteit in Amsterdam. Van 2002 tot 2003 heeft hij gewerkt als AGNIO in het St Elisabeth ziekenhuis te Haarlem en in het VU ziekenhuis te Amsterdam. Zijn opleiding tot cardioloog heeft hij aanvankelijk gestart in het VU ziekenhuis in 2004 en nadien van 2005 tot 2010 in het St Antonius ziekenhuis te Nieuwegein afgerond.
Tijdens zijn opleiding tot cardioloog is hij onder begeleiding van dr. JM ten Berg gestart met onderzoek naar patiënten met obstructieve hypertrofische cardiomyopathy die ofwel behandeld waren geweest met alcohol septum ablatie ofwel met een chirurgische myectomy. Nadat hij vanaf 2011 in het Martini ziekenhuis ging werken als cardioloog heeft hij dit onderzoek voortgezet, nu tevens onder begeleiding van Prof. MP van den Berg van het UMCG Groningen.
Zijn hobby's zijn catamaran zeilen en surfen.
Hij is getrouwd met Valentina Gracchi en heeft twee dochters, Irene en Livia.