Alcohol septal ablation for hypertrophic obstructive cardiomyopathy: focus on safety

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The Rules of Cider House

"*One: Please don't smoke in bed.*"
"*Two: Please don't go up to the roof to eat your lunch.*"
"*Three: Please – even if you are very hot – do not go up to the roof to sleep.*"
"*Four: There should be no going up on the roof at night.*"

John Irving

In this issue of the Swiss Medical Weekly, Streit et al. publish an observational study dealing with safety of alcohol septal ablation (ASA) for hypertrophic obstructive cardiomyopathy (HOCM) [1]. The take-home message of their report is clear. ASA is not only effective but also a safe procedure. The most dreaded complications and consequences of ASA (sudden death, complete AV block and malignant tachyarrhytmias) are not often encountered. Since safety of non-pharmacological therapy of HOCM is in the thick of things now, I would like to comment on several issues raised in their paper and – moreover – to explain some standpoints of both opponents and proponents of this therapeutic approach.

Hypertrophic cardiomyopathy (HCM) is a hereditary cardiac disease with unique pathophysiological characteristics and a great diversity of morphological, functional, and clinical features. HCM is commonly associated with systolic anterior motion of the anterior mitral valve leaflet and increased thickness of the interventricular septum that constitute the main conditions for the left ventricular outflow obstruction (obstructive HCM – HOCM). Typical symptoms are dyspnoea, angina pectoris, palpitations and syncope. Generally, the clinical course of HCM varies markedly and some patients remain asymptomatic throughout life, some have severe symptoms of heart failure or angina pectoris, and others die suddenly often in the absence of previous symptoms. Reported annual mortality is approximately 1% [2].

As shown previously in several studies, the presence of a resting outflow gradient is responsible for many symptoms and probably carries some prognostic significance. Therefore, surgical treatment primarily focused on myectomy of the part of redundant septal myocardium. Until the mid-nineties, surgical myectomy (or extended myectomy with mitral valve repair and partial excision of the papillary muscles) represented the gold standard in the treatment of highly symptomatic patients with HOCM. Surgery markedly reduces the outflow gradient and provides large improvements in objective measures of symptoms and functional status [2–4]. Unfortunately, mortality rates of less than 1 or 2% have only been achieved in exceptional surgical centres with an extensive experience and numerous performed procedures. Moreover, it seems to be probable that many worse surgical results are underreported.

The idea of inducing a septal infarction by endovascular techniques was suggested by the observation of Ulrich Sigwart that myocardial function and outflow gradient could be suppressed by occlusion of the supplying artery during balloon angioplasty. Additionally, the new concept of septal ablation was supported by the old radiological technique with use of alcohol injection to produce necrosis of the targeted tissue. As the first, Ulrich Sigwart published his experience with "non-surgical myocardial reduction" of three patients with HOCM in 1995. He injected several millilitres of pure alcohol into septal branch of the left anterior descending coronary artery to specifically induce limited necrosis of hypertrophied interventricular septum with its subsequent shrinkage and outflow gradient elimination [5]. Since that time several modifications of the original technique have been described and thousands of patients have been treated. Thus, the endovascular septal procedures are several times more frequent than surgical procedures. It is likely that the main reasons for that are as follows: (1) the relatively simple catheteri-

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sation technique, (2) the low procedural risk in experienced hands, (3) preference of the patients, and maybe (4) inclusion of the patients with moderate or mild symptoms. It is of note that there is no evidence for the effect of ASA on survival. Therefore, the procedure should not be performed in asymptomatic or mildly symptomatic patients [2].

ASA has only been examined in one randomised study, which showed both in short- and long-term follow-up that low alcohol dosing (1.5–2 ml) is as similarly effective as "standard" alcohol dose (2–4 ml) [6]. Many observational studies and registries have confirmed the positive effect of ASA on haemodynamics, symptoms, objective measurements of exercise capacity, mitral regurgitation and left ventricular diastolic function [2]. Thus, from the clinical point of view, there is no doubt about the effectiveness of this procedure. However, there is still an ongoing debate on the short- and mainly long-term safety of ASA [3, 4]. This discussion proceeds from the assumption that myocardial necrosis induced as a result ic the procedure might be hazardous and associated with a potential long-term risk of heart failure or sudden death- a good question for clinical research. What do we actually know about the safety of ASA?

First, generally, we should "play by the rule", in other words, "ablate by the rule". Thus, it is advantageous to minimise the extent of myocardial necrosis during ASA. Therefore, (a) we continuously try to find the lowest effective dose of alcohol which might have positive consequences in the long-term follow-up. Based on our clinical experience, we hypothesise that an alcohol dose of about 1 ml injected very slowly (2–5 min.) is likely to be the lowest effective alcohol volume in patients without extreme septum hypertrophy (septum thickness <31 mm) [6–8]. (b) We use echocardiographic contrast medium to delineate the area to be infarcted and to exclude contrast (and subsequently alcohol) deposition in remote myocardial regions [6, 7, 9]; (c) the patient should be observed in coronary care unit for at least 48 hours; (d) similarly, the pacemaker lead should not be removed sooner than two days after the procedure; (e) the onset of delayed complete heart block may occur several days after an uncomplicated procedure. Therefore, telemetric monitoring for the first post-procedural week and prolonged duration of temporary pacemaker backup up to 6 days in patients at high risk (retrograde AV block during electrophysiological examination) should be considered [6–10].

Second, the ASA procedure should be performed only in centres with an extensive experience and a long-term follow-up programme. There is still both a lack of evidence for the optimal technique of the procedure and absence of comparative studies between endovascular and surgical procedures. Hence, more data need to be collected to clarify these relevant issues.

Third, some opponents of ASA claim we try to improve patients' symptoms by generating scar tissue that may be deleterious to long life, and that avoidance of this procedure in young patients is advisable, especially if the surgical option is feasible [3, 4]. However, an electrophysiology report in high-risk patients after ASA has not indicated an increased arrhythmic substrate necessitating higher rates of implanting defibrillators [10]. Although ventricular tachycardia and sudden death have been reported after ASA, it is likely that these events characterise the natural course of HCM irrespective of the treatment option. In this sense, the recent observation by Streit et al. seems to be valuable and shows no significant increase of malignant arrhythmic events following ASA [1].

Four, we should still be aware that ASA is (even in the most experienced centres) associated with some complications. In-hospital mortality ranges in the literature from 1% to 4%, but I strongly believe in centres with the most experience it is less than 1%. Usually complete heart block is transient, however, in recent publications pacemaker implantation is necessary in 5–15% which is several times more frequent than the same complications after myectomy [2].

Five, notwithstanding the differences between the real world of clinical cardiologists and the world of imaginary workers in Irving's Cider House (both in the novel and the film), I feel some similarities do exist. Our goal in the near future should be to develop reliable safety rules for ASA (indications, optimal procedural technique, follow-up). These rules should be evidence-based and defined by cardiologists experienced in ASA. Interestingly, John Irving wrote in his novel and script for the movie The Rules of Cider House: *"Somebody who don't live here made them rules. Them rules ain't for us. We the ones who make up them rules. We makin' our own rules, every day. Ain't that right, Homer?"*

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