The adult mammalian body does retain the robust repair capacity of other species and gradually loses its regenerative potential with age. Our approach has been to intervene in the mechanisms at work in the mammalian response to damage or disease by reducing the impediments to effective regeneration of skeletal and cardiac muscle. In one intervention, transgenic supplementation of a locally acting insulin-like Growth Factor 1 isoform (mIGF-F) promotes efficient tissue repair of damaged skeletal and cardiac muscle without scar formation, and prevents muscle atrophy in hear tfailure. In a second intervention, repression of th eNFkB inflammatory pathway by mIGF-1 in damaged muscle has prompted studies in which mice lacking functional NFkB signaling specifically inskeletal muscle exhibit increased muscle regenerative capacity, wehre as mice lacking NFkB significally in cardiac muscle progressed to failure. In a third intervention, the importance of inflammation to tissue regeneration was explored in a mouse model of impaired macrophage polarization. Taken together, these observations highlight the complexity of recapturing embryonic regenerative capacity by modulating key signaling pathways or cell-tissue interactions in the adult to restore injured or degenerating tissues.

NOTES BY SHARON BATES Email: sharon@anthonybates.org

N. Rosenthal – Science about mouse trails for prevention of dilated Cardiomyopathy.

8:54 Biophysical consequences of sarcomere gene mutations
C. Poggesi (Florence, I)

LECTURE ABSTRACTS

BIOPHYSICAL CONSEQUENSES OF SARCOMERE GENE MUTATIONS

CORRADO POGGESI Email: corrado.poggesi@unifi.it
Department of Physiology, University of Florence, Italy

Mutations in the B-Myosin Heavy Chain gene (MYH7) are among the most frequent sarcomere gene mutations identified as responsible for familial hypertrophic cardiomyopathy (HCM). The functional consequences of these mutations have been extensively investigated using a variety of experimental models and approaches but have never been directly examined in the cardiac sarcomeres of affected patients. We use the single myofibril technique to compare the kinetics of contraction and relaxation of myofibrils isolated from left ventricular samples of patients carrying MYH7 mutations undergoing septal myectomy for severe obstructive HCM with those of control non-HCM patients and healthy donor hearts. Preparations, mounted in a force recording apparatus were Ca^{2+} -activated (pCa 6.0-4.5) and fully relaxed (pCa 8) by rapid (< 5 ms) solutions switching. Myofibrils from HCM patients carrying different MYH7 mutations (R403Q, R692C, R442C) show qualitatively similar changes comared to controls and donors: (i) maximal isometric tension tends to be lower; (ii) Ca^{2+}-sensitivitity of tension generation is higher; (iii) the rate constant of active tension generation follow maximal Ca^{2+} activation is faster; (iv) tension relaxation kinetics upon Ca^{2+} removal are more than twice faster indicating that the apparent rate with which cross-bridges leave their force generating states is accelerated in the HCM preparations. The results suggest that the HCM-associated mutations in Myosin Heavy Chain lead to an apparent gain of protein function but a greater energetic cost of tension generation. The functional impact of mutations of cardiac Myosin binging Protein C and other sarcomere protein genes is under investigation.

NOTES BY SHARON BATES Email: sharon@anthonybates.org

C. Poggesi – Filament research related to the HCM patient on relaxation of heart muscle. They were able to gain HCM filaments from myectomy procedural and a donor heart that was rejected / unused in transplant for control comparison. Interesting but very scientific for me.

9:18 Old genes, new genes and correlations with phenotype
M. Ackerman (Rochester, USA)

LECTURE ABSTRACTS

OLD GENES, NEW GENES AND CORRELATIONS WITH PHENOTYPE

MICHAEL ACKERMAN Email: ackerman.michael@mayo.edu
S.L. Van Driest, V.C. Vasile, S.R. Ommen, M.L. Will, A.J. Tajik, B.J. Gersh, M.J. Ackerman Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic College of Medicine, Rochester, Minnesota, USA

Objectives: We sought to determine the frequency and phonotype of mutations in myosin binding protein C (MYBPC3) in a large outpatient cohort of patients with hypertrophic cardiomyopathy (HCM) seen at our tertiary referral center.
Background: Mutations in MYBPC3 are one of the most frequent genetic causes of HCM and have been

associated with variable onset of disease and prognosis. However, the frequency of mutations and associated clinical presentation have not been established in a large, unrelated cohort of patients.
Methods: Using deoxyribonucleic acid from 389 unrelated patients with HCM, each protein coding exon of MYBPC3 was analyzed for mutations by polymerase chain reaction, denaturing high-performance liquid chromatography, and direct deoxyribonucleic acid sequencing. Clinical data were extracted from patient records blinded to patient genotype.
Results: Of 389 patients with HCM, 71 (18%) had mutations in MYBPC3. In all, 46 mutations were identified, 33 of which were novel (72%). Patients with MYBPC3 mutations did not differ significantly from patients with thick filament-HCM, thin filament-HCM, or genotype-negative HCM with respect to age at diagnosis, degree of hypertrophy, incidence of myectomy, or family history of HCM or sudden death. Patients with multiple mutations (n = 10, 2.6%) had the most severe disease presentation.
Conclusions: This study defines the frequency and associated phenotype for MYBPC3 and/or multiple mutations in HCM in the largest cohort to date. In this cohort, unrelated patients with MYBPC3-HCM virtually mimicked the phenotype of those with mutations in the beta-myosin heavy chain. Patients with multiple mutations had the more severe phenotype.

J Am Coll Cardiol 2004 Nov 2; 44(9): 1903-10

NOTES BY SHARON BATES Email: sharon@anthonybates.org

M. Ackerman – The diseases (HCM) over the cardiac filaments. Thick filaments (old genes) thin filaments are (new genes). Genetic testing available by 4 companies now for the main (most common) 12 HCM mutations. Old Genes – The older young are and the thickness of the septum & the shape of the heart would lead to a negative DNA test for myofilament HCM. What about outcome? Does that matter to the researchers? New Genes – Other type of genes for 2 disc & 1 band or the side of the filaments. These are about 20% of the sigmoidal shaped hearts. Add additional genes -> metabolic HCM genes. Calcium handling protein genes added for HCM. Very Good – All of this becomes target of all genes and new genes are yet to be discovered. The microfilament in mapped. We still have the sarcameare, z-disc, and calcium handling genes to explore. Lots to do for the "R-E-S-P-E-C-T" of research.

9:42 Disease mechanisms in inherited DCM
H. Watkins (Oxford, UK)

LECTURE ABSTRACTS

DISEASE MECHANISMS IN INHERITED DCM

HUGH WATKINS Email: hugh.watkins@cardiov.ox.ac.uk
Department of Cardiovascular Medicine, University of Oxford, UK

Objectives: We sought to determine the frequency and phonotype of mutations in myosin binding protein C (MYBPC3) in a large outpatient cohort of patients with hypertrophic cardiomyopathy (HCM) seen at our tertiary referral center.
Background: Mutations in MYBPC3 are one of the most frequent genetic causes of HCM and have been associated with variable onset of disease and prognosis. However, the frequency of mutations and associated clinical presentation have not been established in a large, unrelated cohort of patients.
Methods: Using deoxyribonucleic acid from 389 unrelated patients with HCM, each protein coding exon of MYBPC3 was analyzed for mutations by polymerase chain reaction, denaturing high-performance liquid chromatography, and direct deoxyribonucleic acid sequencing. Clinical data were extracted from patient records blinded to patient genotype.
Results: Of 389 patients with HCM, 71 (18%) had mutations in MYBPC3. In all, 46 mutations were identified, 33 of which were novel (72%). Patients with MYBPC3 mutations did not differ significantly from patients with thick filament-HCM, thin filament-HCM, or genotype-negative HCM with respect to age at diagnosis, degree of hypertrophy, incidence of myectomy, or family history of HCM or sudden death. Patients with multiple mutations (n = 10, 2.6%) had the most severe disease presentation.
Conclusions: This study defines the frequency and associated phenotype for MYBPC3 and/or multiple mutations in HCM in the largest cohort to date. In this cohort, unrelated patients with MYBPC3-HCM virtually mimicked the phenotype of those with mutations in the beta-myosin heavy chain. Patients with multiple mutations had the more severe phenotype.

J Am Coll Cardiol 2004 Nov 2; 44(9): 1903-10

NOTES BY SHARON BATES Email: sharon@anthonybates.org

H. Watkins – Some genes can create HCM and/or DCM. The identity of the mutations has been specific to the location on the filaments of the heart muscle (good picture).

10:06 Role of functional remodeling in HCM
L. Sartiani (Florence, I)

LECTURE ABSTRACTS

ROLE OF FUNCTIONAL REMODELING IN HCM

LAURA SARIANI Email: laura.sartiani@unifi.it
Department of Pharmacology, University of Florence, Florence, Italy

Remodeling is known to occur in all forms of heart disease. It involves different compartments of heart tissue, including myocytes, the interstitium and the vasculature. The process is initially adaptive and often becomes maladaptive, leading to a progressive decompensation of heart function. This condition is associated to an increased propensity to develop arrhythmias and sudden cardiac death. Of note, the risk of sudden death progresses with heart disease and likely reflects changes in electrophysiological substrate. Animal models of cardiac hypertrophy may be helpful for understanding events occurring in the diseased human heart. In particular, two arrhythmogenic mechanisms have been consistently reported: a prolongation of action potential duration, due to a reduction of repolarizing potassium currents and the expression of the hyperpolarization-activated current, If, interestingly, similar abnormalities have been observed in human cardiomyocytes from human failing hearts.
In human familial Hypertrophic Cardiomyopathy (HCM), myocyte disarray and interstitial fibrosis act as a substrate, alike in acquired cardiomyopathies. Triggers for malignant arrhythmias in HCM are likely represented by cellular electrophysiologic alterations; however, no information exists about these abnormalities in cardiomyocytes from fHCM patients.
Recently, the collaboration with the regional referral center for HCM empowered us to obtain samples from patients undergoing cardiac surgery for obstructive hypertrophy. By using our established electrophysiologic approach, combined with novel molecular and biochemical assays, we investigated the cellular arrhythmogenic mechanisms of HCM and their ionic basis.
While being a genetic disorder, HCM clinical phenotypes (including hypertrophy and sudden death) result from complex interplay among multiple factors. These phenotypes may be seen as secondary, then potentially reversible. However, pathways leading to cardiac remodeling in HCM are largely unexplored, as well as the feasibility of innovative pharmacological strategies aimed to prevent the progression toward end-stage disease. Thus, we focused on some potentially crucial, but ill-investigated mechanisms involved in the alteration of cell metabolism and electrogenesis, by combing studies in samples from HCM patients and in-vitro cell models. From this analysis it will be hopefully possible to identify novel molecular markers of HCM, their role in the progression toward clinical phenotypes and in the appearance of malignant arrhythmias.

NOTES BY SHARON BATES Email: sharon@anthonybates.org

L. Sartiani – The longation of the T-Wave is present in most HCM. What about inverted T-waves what is the correlation to the risk of SCD? Sodium current and late sodium current contributes to the potential of abnormal cells. Functional remodeling is responsible for Ventricle obstruction. Cellular alterations is responsible for cardiac malfunction.

10:45 Coffee Break

NOTES BY SHARON BATES Email: sharon@anthonybates.org

Spoke to Drs. Ommen & Ackerman, Mayo: Spoke to them about our research, posters & screening program in AZ, requesting more support from Mayo Clinic in Scottsdale. Dr. Ommen would like me to send an email (with abstract attachments) asking for support so he will send it forward as an intro to Dr. Tajik in Arizona. Dr. Ommen also knows a former Mayo doctor that went to Cork, Ireland. He will get names to Mary Vesseghi. Also said hello to Dr. Bill McKenna & pointed out my (7) posters.

10:50 **Session 4**
13:15 **HCM clinical management**
Chairmen: **D. Antoniucci** (Florence, I), **I Olivotto** (Florence, I)

DAVID ANTONIUCCI Email: david.antoniucci@virgilio.it
Invasive Cardiology 1, Heart and Vessels Department, Careggi University Hospitals, Florence Italy

IACOPO OLIVOTTO Email: olivottoi@ao-careggi.tosccana.it; iacopo.olivotto@virgilio.it
Referral Center for Cardiomyopathies, Cardiology 1, Heart and Vessels Department, Careggi University Hospital, Florence, Italy

10:50 An overview of contemporary treatment options
F Cecchi (Florence, I)

LECTURE ABSTRACTS

AN OVERVIEW OF CONTEMPORARY TREATMENT OPTIONS

FRANCO CECCHI Email: cecchif@aou-careggi.toscana.it
Referral Center for Cardiomyopathies, Cardiology 1, Heart and Vessels Department, Careggi University Hospital, Florence, Italy

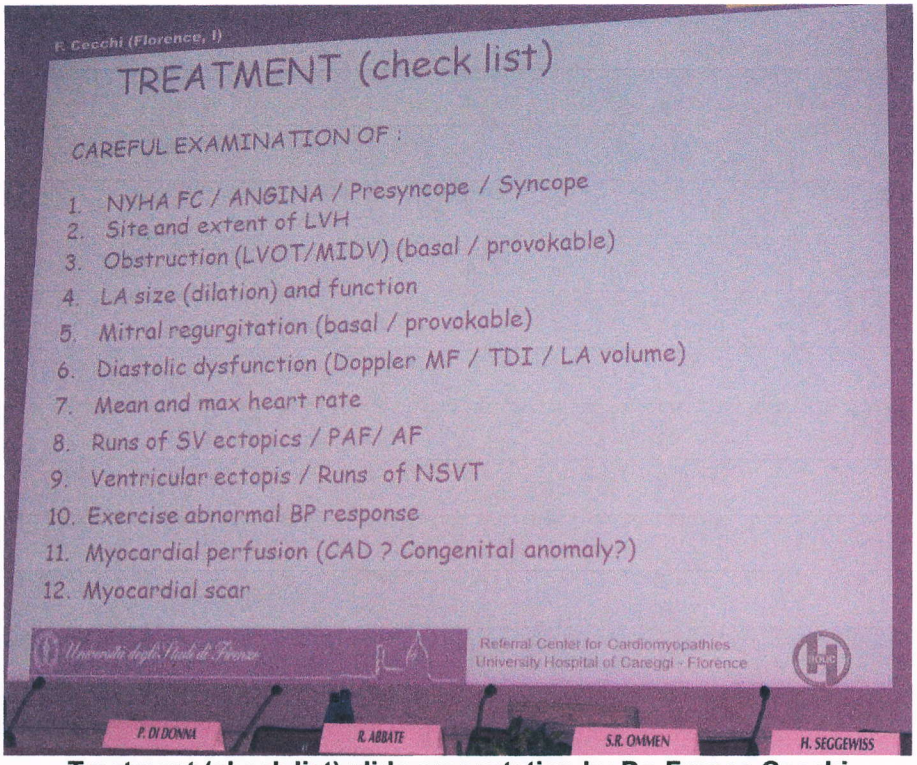
With an estimated prevalence of 1:500, HCM is no more considered a rare disease. It affects a fair number of people in the world. In the last 50 years medical care of HCM patients has greatly improved in most countries. Medical treatment is generally used on empirical basis in order to control symptoms and arrhythmias, slow disease progression, prevent heart failure and sudden death. Differential diagnosis with other causes of LVH, including e.g. supravulvular or fixed subaortic stenosis is anyway necessary. The identification of the genetic or metabolic background, when available and possible, is of great importance for precise characterization of the HCM subtype and specific treatment options. To start appropriate treatment, careful assessment of family history, functional limitation, diastolic and systolic dysfunction, and risk factors, including microvascular disease and fibrosis, basal or inducible intraventricular obstruction and mitral regurgitation, is mandatory. Atrial fibrillation and disease progression are expected in a substantial proportion of patients with HCM, while sudden and unexpected death is usually rare and more difficult to predict. Old and new risk factors should be taken in account. Therapeutic strategy should no longer be limited to control system, but also to reduce the risk of futre complications, including atrial fibrillation, stroke and heart failure. Relief of intraventricular obstruction and mitral regurgitation by cardiac surgery or other interventional approaches may be greatly beneficial for symptom control and minor risks. Evidence for increased survival has only been demonstrated for extended myectomy. Medical treatment is anyway necessary, and usually patients refer symptom improvement with beta-blockers (e.g. Nadolol), when mild symptoms and functional limitation are present. Beta-blockers and Amiodarone are often beneficial when arrhythmias occur, both for treatment and prevention. In more advanced disease stages, standard heart failure treatment including CRT or transplant in the end-stage phase, is the treatment of choice. Although transgenic animals have shown to benefit prophylactic treatment with diltiazem or ARB in order to avoid or reduce fibrosis and disease progression, no evidence has been produced as yet in humans.

MEDICAL THERAPY

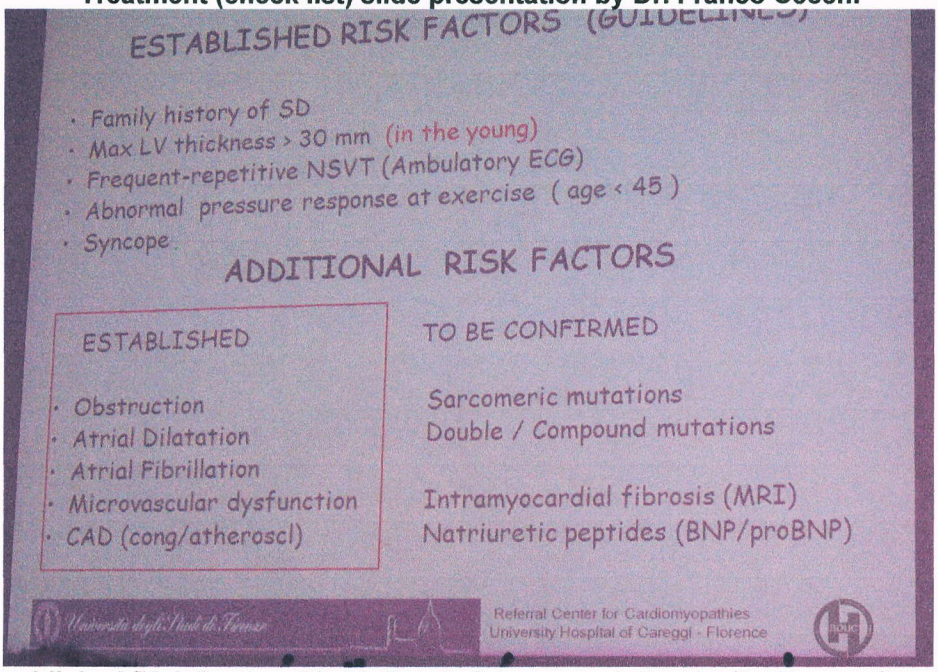
Intraventricular obstruction	Angina and Ischemia
Beta-blockers (e.g. Nadolol 40-240 mg)	Beta-blockers + Channel-blockers (e.g. Felodipine)
Disopyramide (250-750 mg)	
Beta-blockers + Disopyramide	Heart Failure
	Beta-blockers (Carvedilol, bisoprolol),
Arrhythmias (AF; VEB; nsVT)	Amiodarone (low dose),
Amiodarone (low dose)	Furosemide
Beta-blockers + Amiodarone (low dose)	ACE-I, ARB, Nitrates
Pacing, CRT when needed	

NOTES BY SHARON BATES Email: sharon@anthonybates.org

F. Cecchi – Challenges in modern medicine, HCM w/ varied needs. Italy has an HCM registry (1600 patients). Afib 22% is most CV events to prevent besides disease progression (a symptomatic to symptomatic). Careful examination of symptoms & risk factors.



Treatment (check list) slide presentation by Dr. Franco Cecchi



Established Risk Factors (Guidelines) slide presentation by Dr. Franco Cecchi

10:50 State-of-the-art management of atrial fibrillation and ventricular arrhythmias
P DiDonna (Massala, I)

LECTURE ABSTRACTS

STATE-OF-THE-ART MANAGEMENT OF ATRIAL FIBRILLATION AND VENTRICULAR ARRHYTHMIAS

PAOLO DI DONNA Email: didonna@asl.at.it
F. Gaita, P. Di Donna
University of Turin and Cardiology Department of Asti, Civil Hospital Cardinal Massala, Italy

Atrial fibrillation (AF) is a common arrhythmia, increasing with age, with as many as 4% of people 60 to 65

years of age, and 10% of those ≥ 80 years of age affected. AF is associated with substantial mortality and morbidity from stroke, thromboembolism, heart failure, and impaired quality of life[1-2]. The management of patients with AF should broadly be guided by symptoms, the presence or absence of haemodynamic compromise and associated comorbidities[3]. In patients given a rate control strategy, the objective is heart rate control of the ventricular response and hence, drugs or non pharmacological approaches are used. For rhythm control in patients with paroxysmal AF the objective is the reduction of episodes and the long term maintenance of sinus rhythm (drugs or non pharmacological approaches). In persistent AF the management objective is the sinus rhythm restoration and hence, cardioversion pharmacological or electrical is attempted. Irrespective of clinical subtype of AF, appropriate antithrombotic treatment is mandatory, based on risk factors for stroke and thromboembolism. Several clinical trails[4-5] comparing rhythm control with rate control have shown no significant differences between the two strategies for AF. However a non significant trend was seen for excess mortality with rhythm control approach in the AFFIRM trial, for functional endpoints some trials showed improvement in exercise capacity[5]. In these studies traditional pharmacologic approach to maintain sinus rhythm in patients with AF have been disappointing with long-term recurrence rates of approximately 50%, regardless of the specific antiarrhythmic drug chosen[6-7]. Furthermore, side effect, including proarrhythmia, are common. For these reasons, great effort has been made to develop non-pharmacological treatments of AF. These have included atrioventricular node ablation with permanent pace-making insertion, but this approach does not restore sinus rhythm and needs chronic anticoagulation. Surgical approaches to AF are effective options for those patients requiring open heart surgery for valvular heart diseases[8]. More recently, key insights into the mechanism of AF initiation and maintenance, have ushered in the field of catheter ablation of AF, providing a treatment directed to eliminate the triggers and to modify the substrate as potential cure for AF in a sizable proportion of patients. Over the last decade, transcatheter techniques for ablation of AF have been successfully introduced in clinical practice[9-11]. Actually AF ablation could be considered in symptomatic patients who have been resistant or intolerant to pharmacological treatment, especially those who are younger, have lone atrial fibrillation and with congestive heart failure. However, the feasibility and efficacy of these techniques in patients with genetically determined myocardial disease, such as hypertrophic Cardiomyopathy (HC), is largely unknown[12-13]. Recently, we published results of our study aimed to evaluate the feasibility, safety and efficacy of radiofrequency ablation of AF in HC patients[14]. An ablation scheme with pulmonary vein isolation plus linear lesions. "7" scheme, was employed in patients with HC and AF refractory to pharmacological therapy and with haemodynamic compromise and clinical impairment. Twenty-six HC patients from three referral institutions (Asti, Florence and Turin) with paroxysmal (n = 13) or permanent (n = 13) AF, refractory to antiarrhythmic therapy (age 58 ± 11 years, left atrial volume 17 0 ± 48 ml) underwent radiofrequency catheter ablation.

No major peri-procedure complications occurred; 1 patient died of hemorrhagic stroke four weeks after catheter ablation, while in sinus rhythm. During a 19 ± 10 month follow-up, 9 of the remaining 25 patients (36%) had AF recurrence (despite repeat procedure in 3), and were considered as failures, whereas 16 remained in sinus rhythm (i.e. a 64% overall success rate). Ten of these 16 patients were off antiarrhythmic drugs at final evaluation. However despite these encouraging results, few patients have been treated and the follow-up is short so that firm conclusions cannot be drawn. Extending the experience from AF ablation in structural heart disease to patients with clinical course is heterogeneous. It appears therefore essential performing specific ablation studies in patients with AF and HC before launching the procedure in a large scale.

Sustained ventricular tachycardia (VT) is an important cause of morbidity and sudden death in patients with heart disease. Implantable cardioverter defibrillator (ICDs) terminate VT episodes, reduce the risk of sudden death but recurrent VT develops in 40 to 60% of patients. ICD shocks reduce quality of life and are associated with an increased risk of death[15]. Antiarrhythmic therapy with amiodarone and sotalol reduces VT episodes but with disappointing incidence of side effects and efficacy. Catheter ablation is useful for reducing VT episodes and can be life saving in cases when incessant. Idiopathic VTs occur in patient without structural heart disease, generally young and are rarely associated with sudden death.

The most common forms have a focal origin in the right ventricle or left ventricle out-flow regions[16]. Electrophysiological study is often warranted to confirm the diagnosis and often to cure arrhythmia. ECG types of VT often suggest its likely cause and associated heart disease. Monomorphic VT has the same QRS complex from beat to beat, indicating repetitive ventricular activation from a structural substrate or focus that can be targeted for ablation. Most are due to reentry through regions of ventricular scar. Ventricular activation in polymorphic VTs is changing due to functional reentry without structural targeted for ablation as in myocardial ischemia, long-QT syndrome and a number of genetic syndromes which are causes. The field in the diagnosis and treatment of AF and VT continues to benefit from clinical studies and technological developments. Electrophysiological approaches could hold some promise for a

curative approach in AF and should be considered in the therapeutic armamentarium for treatment of recurrent VT.

References
1) Loyd-Jones DM, Wang TJ, Leip EP, et al. Lifetime risk for development of atrial fibrillation; the Framingham heart study. Circulation 2004; 100: 1042-46.
2) Fuster V, Ryden LE, Assinger RW, Cannom DS et al. American College of Cardiology/American Heart Association Task Force on Practice Guidelines; European Society of Cardiology Committee for Pracitice Guidelines for the Management of patients with Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology Committee for practice guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients with Atrial Fibrillation): Developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society, Circulation 2006; 104: e257-e354.
3) Lip GY, Tello-Montoliu A. Management of atrial fibrillation. Heart 2006; 92: 1177-82.
4) Wyse DG, Waldo AL, DiMarco JP, et al; Atrial Fibrillation Follow-up investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med 2002; 347(23): 2815-33.
5) Singh SN, Tang XC, Singh BN, et al; for the SAFE-T investigators. Quality of life and exercise performance in patients in sinus rhythm verses persistent atrial fibrillation in a veterans affairs cooperative studies program substudy. J Am Coll Cardiol 2006; 48: 721-30.
6) Crjins HJ, Van Gelder IC, Van Gilst WH, et al. Serial antiarrhythmic drug to maintain sinus rhythm after electrical cardioversion for chronic atrial fibrillation or atrial flutter. Am J Cardiol 1991; 68: 335-41.
7) Roy D, Taljic M, Dorian P, et al. Amiodarone to prevent recurrence of atrial fibrillation. Canadian Trial of Atrial Fibrillation Investigators. N Engl J Med 2000; 342: 913-20.
8) Gaita F, Riccardi R, Caponi D, et al. Linear cryoablation of the left atrium versus pulmonary vein cryoisolation in patients with permanent atrial fibrillation and valvular heart disease; correlation of electroanatomic mapping and long-term clinical results. Circulation 2005; 111(2): 136-42.
9) Haissaguerre M, Jais P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998; 339(10): 659-666.
10) Haissaguerre M, Jais P, Shah DC, et al. Electrophysiological end point for catheter ablation of atrial fibrillation initiated from multiple pulmonary venous foci. Circulation 2000; 1001(12): 1409-17.
11) Oral H, Scharf C. Chugh A, et al. Catheter ablation for paroxysmal atrial fibrillationL segmental pulmonary vein oastial ablation versus left atrial ablation. Circulation 2003; 108(19): 2355-60. Epub 2003 Oct 13/
12) Chen MS, McCarthy PM, Lever HM, Smerdira NG, Lytle BL. Effectiveness of atrial fibrillation surgery in patients with hypertrophic Cardiomyopathy. Am J Cardiol 2004; 93(3): 373-5.
13) Liu X, Ouyang F, Mavrakis H, et al. Complete pulmonary vein isolation guided by three dimensional electroanatomical mapping for the treatment of paroxysmal atrial fibrillation in patients with hypertrophic obstructive Cardiomyopathy. Eropace 2005; 7(5): 421-7.
14) F Gaita, P DiDonna, I Olivotto, et al. Usefulness and safety of transcatheter ablation of atrial fibrillation in patients with hypertrophic cardiomyopathy. Am J Cardiol 2007; 99: 1575-1581.
15) Moss AJ, Greenberg H, Case RB, et al. Long term clinical course of patients after terminatioin of ventricular tachyarrhythmia by an implanted defibrillator. Circulation 2004; 110: 3760-3765.
16) Tada H, Ito S, Naito S, et al. Idiopathic ventricular arrhythmia arising from the mitral annulus; a distinct subgroup of idiopathic ventricular arrhythmias. J Am Coll Cardiol 2005; 45: 877-886.

NOTES BY SHARON BATES Email: sharon@anthonybates.org

P. Di Donna – Use of alcohol ablation in 44 patients and the findings & follow-up. More long term follow-up is required. Patients with AF severe seem to be on the down turn of their life. Bi-ventricular pacing patients in end stage – improvements were noted. Technology & knowledge must work together for the future.

11:38 Prevention of systemic embolism: old and new drugs
R Abbate (Florence, I)

LECTURE ABSTRACTS

PREVENTION OF SYSTEMIC EMBOLISM: OLD AND NEW DRUGS

ROSANNA ABBATE Email: rosanna.abbate@unifi.it
R. Abbate[1], E. Cecchi[1,2]
[1]Department of Medical and Surgical Critical Care, Thrombosis Centre, University of Florence, Heart and Vessels Department, Careggi University Hospital, Florence, Italy, [2]Don Carlo Gnocchi Foundation, IRCCS, Florence, Italy

Patients affected by cardiomyopathies may experience systemic embolism either for the occurrence of atrial fibrillation (AF) or for left ventricular thrombus formation. AF is the most common sustained arrhythmia in hypertrophic cardiomyopathy (HCM) and usually justifies aggressive therapeutic strategies. Paroxysmal episodes of chronic AF ultimately occur in about 25% of HCM patients and are mainly determined by left atrial enlargement; subclinical AF may be even more common. Since even one or two episodes of paroxysmal AF have been associated with increased risk for systemic thromoembolism in HCM patients, the threshold for initiation of anticoagulant therapy should be low. Warfarin is the recommended antiocoagulant agent in HCM patients judged to be at risk for thromoembolism. While antiocoagulant reduces the risk of thromoembolic events in HCM patients with AF, it is also recognized

that this therapy does not completely abolish the risk of stroke. Such clinical decisions should be tailored to the individual patient after considering the risk for hemorrhagic complications, lifestyle modifications and expectations for compliance. New studies are ongoing to evaluate the possible role of other oral anticoagulants in patients with AF. Ximelagatran, a direct thrombin inhibitor, was not marketed further due to its potential side-effects; the related compound dabigatran was recently approved in th eeuropean Union. Together with rivaroxaban, the related factor Xa-inhibitor apixaban and LY517717 are under development as non-monitored antithrombotic drugs. However, their possible employment in the prevention of systemic embolism in patients with AF, needs a further assessment in particular in the subgroup of patients with HCM.
In conclusion, in view of the devastating consequences of systemic embolism, the documented effectiveness of antithrombotic therapy in high-risk HCM patients, such as those with AF, and the improved safety of long-term anticoagulant treatment in recent years, it may be prudent to use antithrombotic treatment unless contraindicated.

NOTES BY SHARON BATES Email: sharon@anthonybates.org

R. Abbate – Study on anti coagulation drugs. Still no near market to replace current drugs, but a list of "best practice" shows oral, no labs, direct benefit to reduce risks of current drugs with side affects and conflict to food or other drugs.

Round Table
How to relieve LVOT obstruction

12:02 Lessons learned from four decades of surgical myectomy
S.R. Ommen (Minneapolis, USA)

LECTURE ABSTRACTS

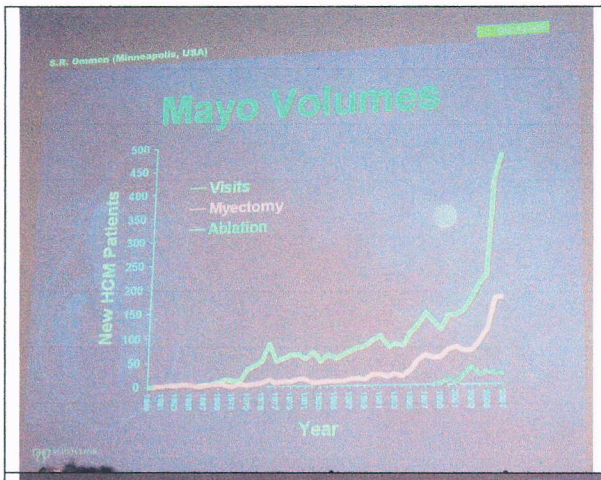
LESSONS LEARNED FROM FOUR DECADES OF SURGICAL MYECTOMY

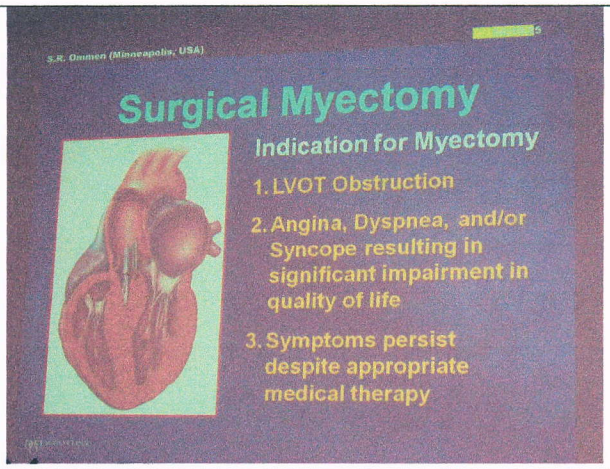
STEVE R. OMMEN Email: ommen.steve@mayo.edu
Division of Cardiovascular Diseases, Mayo Cardiomyopathy Clinic, Rochester, USA

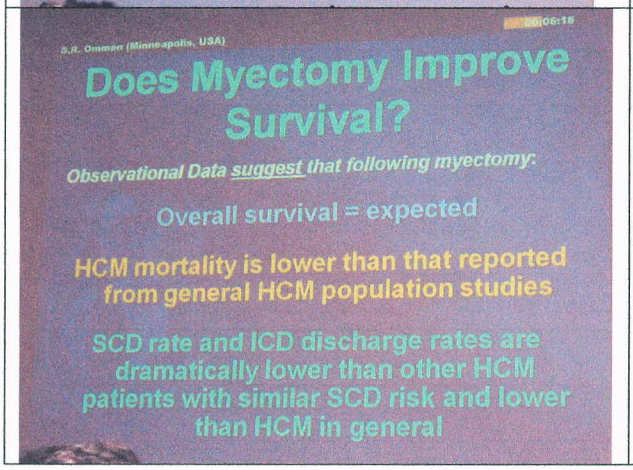
Surgery for the relief of left ventricular outflow tract obstruction has been the subject of extensive research and considerable controversy over the history of the disease now known as hypertrophic cardiomyopathy (HCM). Many of the initial case series were surgical series with significant morbidity and mortality accompanied by statements that operations should be avoided. Since that time, modifications of the myectomy procedure, improvements in the field of cardiac surgery, and improvements in the understanding of the hemodynamics of obstructive HCM have led to the modern era where myectomy performed in centers with expertise in the medical and surgical management of HCM, operative mortality is very small (< 1%), complication rates are low (2 – 3%), gradient relief is robust and durable, and significant symptom relief occurs in 90-95% of patients. Data now points to the possibility of a survival and sudden cardiac arrest benefit among eligible patients. Surgical myectomy has been a prominent feature throughout the 50 year history of HCM, and remains as the gold-standard, definitive method for relief of drug-refractory symptoms in obstructive HCM.

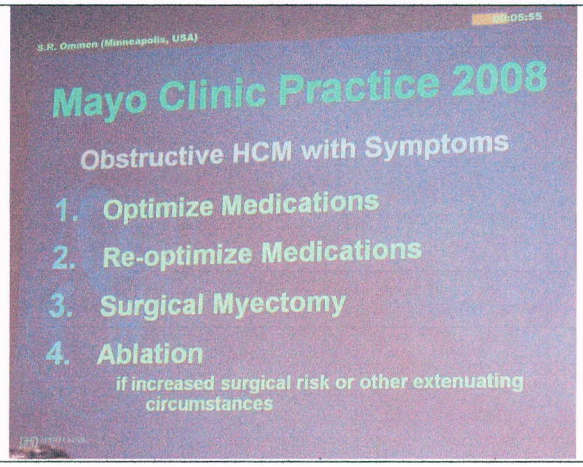
NOTES BY SHARON BATES Email: sharon@anthonybates.org

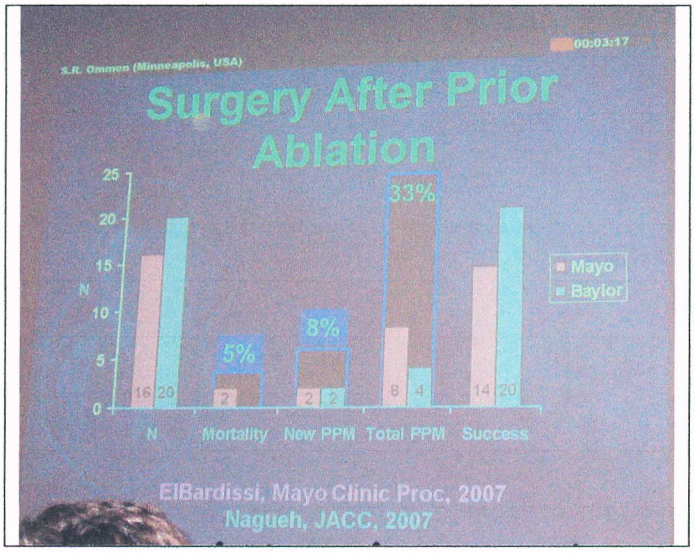
S.R. Ommen – Why do we operate? Improve symptoms, save lives. Only 2% repeat procedure, some for normal growth (younger than 15 at the time of 1st myectomy) or other procedures were done elsewhere. What about MR – some repairs are necessary.
Patients with obstruction have a more likely higher mortality rate after surgery this life expansion improves significantly.











Various pictures from Dr. Steve Ommen's presentation lecture on the last decade on Myectomy.

12:17 Lessons learned from a decade of alcohol septal ablation
H. Seggewiss (Schweinfurt, D)

LECTURE ABSTRACTS

LESSONS LEARNED FROM A DECADE OF ALCOHOL SEPTAL ABLATION

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Percutaneous septal ablation (PTSMA) was introduced as an alternative treatment for symptomatic patients with hypertrophic obstructive cardiomyopathy. After the recognition of its effectiveness and the low complication rate, the induction of a localized therapeutic myocardial infarction due to alcohol-induced septal branch occlusion has been applied also to younger patients. The technique of PTSMA has been refined, with the intention to improve the identification of the target septal perforator branch, in order that the optimal hemodynamic result with the less complications is achieved. In order to identify the target septal branch and to exclude alcohol injection to a wrong area, e.g. papillary muscle or the left ventricular free wall, transthroacic echocardiographic monitoring of the procedure is routinely performed. Indications for percutaneous septal ablation involve symptomatic patients NYHA III/CCS III despite optimal drug therapy or with substantial side effects from medication. Patients with less severe symptoms should only be treated if they have high outflow tract gradients ($\geq$ 30 mmHg at rest or $\geq$ 60 (100) mmHg under stress) and objective reduction of exercise capacity. Nevertheless, it should be taken into consideration that no data hitherto suggests that gradient reduction reduces the risk of sudden death, although a resting gradient more than 30 mmHg has been correlated with a higher risk for sudden death. Patients with previous, but hemodynamically unsuccessful, surgical myectomy or DDD pacemaker implantation can also be treated with alcohol ablation. On the other hand, patients with concomitant cardiac diseases indicating surgery, e.g. valvular disease, and morphologic changes of the mitral valve as well as papillary muscle responsible for gradient formation or mitral regurgitation, should be referred for myectomy. The overall results of percutaneous septal ablation are very satisfactory with a significant reduction of LVOT gradient in approximately 90% of patients in the short term. Mortality rates range from 0 to 4%, while the most frequent complication, AV conduction block, requires permanent pacemaker implantation in less than 10% of the treated patients. Moreover, the early and intermediate results of percutaneous septal ablation are comparable to those after myectomy. It should be considered, however, that younger patients seem to have lower LVOT gradient reduction after the procedure. This may be attributed to the high degree of collateralization of the septum. Furthermore, a presumably higher degree of fibrosis, as opposed to muscle tissue hypertrophy, in the frequently markedly thickened septal ablation. Advances in tissue characterization would probably help in the future to distinguish muscle from fibrotic tissue, thus enabling a more efficient pre-interventional indication. Up to now, no randomized trials comparing surgical and percutaneous treatment of septal reduction in HOCM have been published. Non-randomized trials have shown significant reduction of LVOT obstruction and symptomatic improvement by both treatment options. Therefore, benefits and drawbacks for each therapeutic method must be counterbalanced when deciding on treatment for LVOT obstruction. This decision has to take into consideration several clinical, morphological, and technical aspects. The advantages of percutaneous septal ablation comprise the avoidance of cardiopulmonary bypass with attendant risks, especially in elderly patients with concomitant non-cardiac disease, as well as shorter hospital stay and recovery time. Nevertheless, it must be taken into consideration that too short hospitalization may include the risk of late out-of-hospital heart block as pointed out. Furthermore, the percutaneous approach is less expensive. Potential drawbacks of PTSMA in comparison to myectomy are the risk of damage to the left coronary artery requiring emergency bypass surgery or left main / LAD stenting and the technical impossibility of reaching or identifying a target septal branch.

In these patients elective myectomy can be performed. Furthermore, mitral valve leaflet and papillary muscle abnormalities can avert a good result after septal ablation. In addition, younger patients with large septal thickness have to be informed about the possibility of less frequently successful ablation. On the other hand, it could be shown, in contrast to previous ideas, that even patients with isolated mid-cavitary or combined subaortic and midcavitary obstruction can be successfully treated by echo-guided percutaneous septal ablation. Advantages of myectomy surgery comprise more immediate and complete relief of resting and provoked obstruction and concomitant mitral regurgitation in addition to the good long-term results up to 40 years in contrast to 12 years follow-up results after percutaneous septal ablation. Although there is no reisk of coronary dissection or unwanted myocardioal infarction, most surgical series report on a low risk of aortic regurgitation after surgery. Arrhythmogenic effects after myectomy have not been described. While there are some reports of successful combined simultaneous or stage percutaneous treatment of HOCM and coronary artery disease surgery includes the ability to deal with HOCM and coexistent cardiac disease such as coronary artery disease, valve replacement, right ventricular obstruction, constricting muscle bridges over the left anterior descending coronary artery, and atrial fibrillation.

Overall, PTSMA has been acknowledged as an alternative to surgical therapy in terms of safety as well as morphological and clinical efficacy in hypertrophic obstructive Cardiomyopathy. Intral-procedural echocardiographic monitoring with the use of echo-contrast agents is an essential part of the technique and results in optimization of the septal area to be ablated, thus leading to reduction of peri-interventional