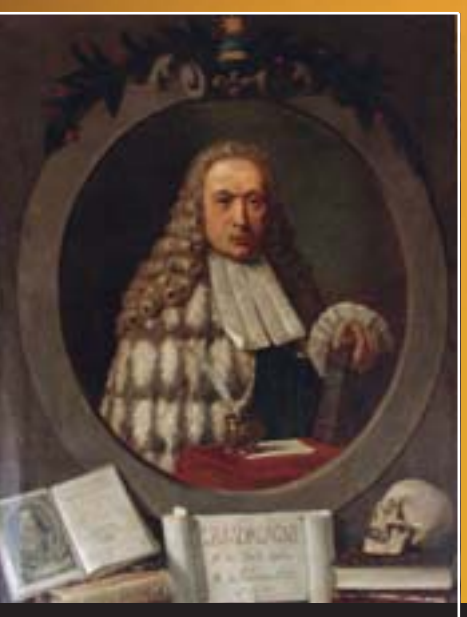
1st Biannual Meeting of the



ASSOCIATION for EUROPEAN CARDIOVASCULAR PATHOLOGY

Congress Venue
Abbazia di Praglia
Via Abbazia, 7
Bresseo di Teolo, Padua, Italy

October 21-23, 2004

UNIVERSITY OF PADUA

A.N.M.C.O.

E.S.C.-WG17

FACULTY OF MEDICINE, UNIVERSITY OF PADUA

G.S.I.P.C.

S.I.A.P.E.C.-I.A.P.

S.I.C.

THURSDAY OCTOBER 21, 2004

09:00 **VULNERABLE PLAQUE**
Plaques at high risk of myocardial infarction and sudden death
A. Van der Wal, Amsterdam-NL
Triggers and clinical markers of acute coronary syndromes
F. Crea, Roma-I
In vivo detection of vulnerable plaque: invasive imaging
R. De Caterina, Chieti-I
In vivo detection of vulnerable plaque: non invasive imaging
J. Narula, Orange-USA
Interventional treatment of acute coronary syndromes
B. Reimers, Mirano Venezia-I

12:15 **Key note lecture** Experimental Atherogenesis
H-A. Lehr, Mainz-D

17:00 **OPENING CEREMONY AND MASTER LECTURE**
Aula Magna, Palazzo del Bo'
Therapeutic weapons against atherothrombosis
V. Fuster, New York-USA

FRIDAY OCTOBER 22, 2004

09:00 **HEART VALVE DISEASE**
Surgical anatomy of cardiac valves
A. Cook, London-UK
The current pathology spectrum of valve disease
P. Bruneval, Paris-F
Clinical non–invasive assessment of heart valve disease: morphological and functional aspects
R. Scognamiglio, Padua-I
Surgical treatment: valve repair
O. Alfieri, Milan-I
Surgical treatment: valve replacement and outcome
G. Gerosa, Padua-I

17:00 **Key note lecture** Advances in cardiovascular imaging
R. Fattori, Bologna-I

SATURDAY OCTOBER 23, 2004

09:00 **STEM CELLS** *Joint Symposium of the Association for European Cardiovascular Pathology and Society for Cardiovascular Pathology*
Development of cardiac muscle cell diversity
A. Moorman, Amsterdam-NL
Human and mouse stem cells in repair of the injured heart: functional aspects
C. Murry, Seattle-USA
Endothelial and smooth muscle progenitor cells and their roles in tissue regeneration
R.N. Mitchell, Boston-USA
Factors affecting functional outcome after autologous skeletal myoblast transplantation
J-T. Vilquin, Paris-F
Infarct remodelling after intramyocardial progenitor cell injection treatment in patients with acute myocardial infarction
C. Stamm, Rostock-D

12:30 **Key note lecture** Molecular genetics of sudden death
G.A.Danieli, Padua-I

Ministero della Salute

E.C.M.

For Italian Participants Only
The Meeting has been registered for Continuing Medical Education of the Italian Ministry of Health and obtained **16 credit hours**. Number of participants is limited to 50.

PRESIDENT
Anton E. Becker, *Amsterdam-NL*

PROGRAM COMMITTEE CHAIR
Patrick J. Gallagher, *Southampton-UK*

LOCAL ORGANIZING COMMITTEE
Gaetano Thiene, chair

Annalisa Angelini
Cristina Basso
Fiorella Calabrese
University of Padua Medical School, Padua - I

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WELCOME MESSAGE

It is a great pleasure to welcome the European scientists working in the field of cardiovascular pathology. The Association for European Cardiovascular Pathology, recently founded, will held in the Abbey of Praglia the first biannual Meeting, with 3 days of full immersion of Symposia, Free communications and Posters. A Joint Symposium has been planned with the Society for Cardiovascular Pathology, which is the "sister" society on the other side of the Atlantic Ocean.
It is particularly a great honour for the University of Padua to give hospitality to this scientific event, considering that anatomy, phisiology and pathology of the heart and great vessels first developed in this old gymnasium in the XVI-XVIII centuries, thanks to the contributions of Andreas Vesalius, William Harvey and Giovanni Battista Morgagni. The tradition of the study and treatment of cardiovascular diseases culminated recently in the heart transplantation, carried out in Padua for the first time in Italy in 1985, which resulted in the turning of the role of the cardiac pathologist from postmortem to in vivo investigation.
Pathology evolved tremendously in the last decades with the advent of immunohistochemistry and molecular biology, to play a crucial role both in the care of the patient and in basic science research. Keeping the pace of clinical advances represents the major challenge for the pathologist, especially in the field of cardiovascular diseases which are the major causes of morbility and mortality in the Western countries.
I wish all the attendants stimulating and fruitfull scientific debates as well as a pleasant stay in the Euganei Hills of Francesco Petrarca and Tito Livio.

Gaetano Thiene
Chairman,
Local Organizing Committee

AECVP COUNCIL

OFFICERS

Anton E. Becker , *Amsterdam-NL*	President
Gaetano Thiene, *Padua-I*	Vice-President
Allard C. van der Wal, *Amsterdam-NL*	Secretary Treasurer

COUNCIL MEMBERS

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Hans-Anton Lehr, *Mainz-D*
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Nominating Committee

Margaret Burke, *Harefield-UK*	Chair
Ulrik Baandrup, *Aarhus-DK*	
Mat J.A.P. Daemen, *Maastricht-NL*	

GENERAL INFORMATION

DATES and VENUE:

From Thursday 21 October to Saturday 23 October 2004.

The Meeting will take place in the Benedictine Abbey of Praglia, that lies at the foot of the Euganean Hills, 12 km from Padua.

How to reach Praglia
It is easily accessible by car and bus service.
The Venice-Marco Polo Airport is close to Padua approximately 30 minutes and the most convenient way to reach the Congress venue is by using the bus service.
– from Venice Airport: take the bus ACTV for Teolo (that stop also at the Padua station).
– from Padua Railway Station: 5 minutes walk to the SITA Bus Station, take the bus for Teolo-Vò-Noventa Vicentina (bus stop: Praglia)

Otherwise, by car:
– from Venice: highway A4 Milano-Venezia, Padova Ovest exit. Proceed toward Terme Euganee and then to Colli Euganei (km.18);
– from Bologna: highway A13 Padova-Bologna, Terme Euganee exit, toward Montegrotto Terme, Colli Euganei, Monterosso (km.14)

OFFICIAL LANGUAGE:

The official language of the Meeting is English.

REGISTRATION FEE:

Members	waived
Non members	Euro 120
Young investigators (<35 yrs)	waived
Lunch is not included in the registration fee, that will cost	Euro 25 each

ACCREDITATION:

The meeting has been registered for Continuing Medical Education of the Italian Ministry of Health and obtained 16 credit hours.

FOR ITALIAN PARTICIPANTS ONLY:

L'accreditamento è stato richiesto per la sola categoria dei medici per un numero limitato di 50 partecipanti. Ai fini dell'attestazione dei crediti formativi ECM è necessaria l'effettiva presenza al 100% di tutte e tre le giornate con riconsegna al termine del congresso della documentazione debitamente compilata e firmata. La rilevazione della presenza avverrà tramite firma su modulo cartaceo disponibile presso il Desk Segreteria.

BADGES:

Name badges will be needed for admission to the scientific sessions. Please, wear your badge visibly.

DELEGATE BRIEFCASES:

Please ensure that your briefcase is clearly labelled with your name or business card.

CERTIFICATE of ATTENDANCE:

Certificate of attendance will be available at the Registration Desks on Saturday 23 October.

TRANSFER SERVICE:

During the days of the meeting, transfer service will be provided to the registered participants by bus from Abano Terme to Praglia in the morning and back to Abano Terme at the end of each daily programme. More information will be available at the Secretariat Desk during the meeting.

CLIMATE:

The temperature in October is approximately 15°C in the daytime, but cooler at night.

SOCIAL PROGRAM:

Thursday, October 21, 2004 – h. 17:00	
Visit to Palazzo del Bo' and Anatomical Theatre	waived
Friday, October 22, 2004 – h. 21:00	
Congress Dinner	euro 50

POST-CONGRESS PROGRAM:

Sunday, October 24, 2004	
Tour to Venice Laguna Islands and lunch at the Cipriani Locanda in Torcello	euro 120

09:00 Registration

SYMPOSIUM VULNERABLE PLAQUE
Chairpersons: A.E. Becker, Amsterdam-NL; S. Iliceto, Padua-I

10:00 Plaques at high risk of myocardial infarction and sudden death S01
A. Van der Wal, Amsterdam-NL

10:20 Triggers and clinical markers of acute coronary syndromes S02
F. Crea, Roma-I

10:40 In vivo detection of vulnerable plaque: invasive imaging S03
R. De Caterina, Chieti-I

11:00 In vivo detection of vulnerable plaque: non invasive imaging S04
J. Narula, Orange-USA

11:20 Interventional treatment of acute coronary syndromes S05
B. Reimers, Mirano Venice-I

11:40 DISCUSSION

12:15 **Key note lecture**
Chairperson: A. Angelini, Padua-I
Experimental Atherogenesis S06
H-A. Lehr, Mainz-D

13:00 LUNCH AND VISIT TO POSTERS
Chairperson: *S.K. Suvarna, Sheffield-UK*

P01 Macroscopical and microscopical characteristics of pulmonary veins ostia and atrial fibrillation (*I.Kholova, J.Kautzner; Kuopio-FIN)*

P02 Infarct-related artery occlusion, tissue markers of ischemia, and increased apoptosis in the peri-infarct viable myocardium (*A.Abbate, G.G.L.Biondi Zoccai, C.Morales, R.Bussani, D.Santini, R.J.Gelpi, F.Silvestri, F.Baldi, L.M.Biasucci, A.Baldi; Naples-I, Rome-I, Buenos Aires-RA, Trieste-I)*

P03 Parental cigarette smoke as a risk factor for early coronary artery disease and sudden unexpected perinatal and infant death (*L.Matturri, G.Ottaviani, R.Mingrone, M.Mauri, A.M.Lavezzi; Milan-I)*

P04 The "Cardiovascular Registry" at the University of Padua: preliminary results from the anatomical collection of acquired heart-vessels disease (*A.Abdureheman, C.Basso, G.Thiene; Padua-I)*

P05 Myocardial perfusion grade and survival after percutaneous transluminal coronary angioplasty in patients with cardiogenic shock (*G.Tarantini, P.Buja, A.Ramondo, M.Napodano, C.Bilato, G.B.Isabella, R.Razzolini, S.Iliceto; Padua-I)*

THURSDAY OCTOBER 21, 2004

P06 Late results on survival and rehospitalization in patients undergoing different treatment for severe ischemic mitral regurgitation with multivessel coronary artery disease (*P.Buja, G.Tarantini, F.DelBianco, M.Napodano, G.Isabella, R.Razzolini, A.Ramondo, G.Gerosa, S.Iliceto; Padua-I)*

P07 Alveolar gas exchange improvement in prevention of adrenaline-induced myocardial injury (*V.A.Ohanyan, A.B.Semerjyan; Yerevan-AR)*

P08 Myocardial production and secretion of chromogranin A in hypertrophic cardiomyopathy (*M.Pieroni, C.Chimenti, A.Santagostino, A.Maseri, A.Corti, A.Frustaci; Milan-I, Rome-I)*

P09 Association of the T-786 C endothelial nitric oxide synthase Snp with cardiovascular mortality in high risk men (*G.Maiolino, M.Zanchetta, D.Sticchi, M.Cesari, L.Pedon, A.C.Pessina, G.P.Rossi; Padua-I, Cittadella Padua-I)*

P10 Histological vascular patterns of lower limb amputations in hemodialysis patients (*R.Gouveia, R.Birne, T.Adragao, A.Pina, J.Nogueira, M.J. M.J.Pais, H.Messia, A.P.Martins; Lisboa-P)*

P11 Lipid rich atheromatous core with thin fibrous cap as a determinant for neointimal formation among in-stent restenosis (*H.Ishibashi-Ueda, K.Ohta, H.Hao, Y.Ikeda, M.Yamagishi, C.Yutani; Osaka-J)*

P12 Plaque haemorrhage, atheroma and C-reactive protein: an "in vivo" study in stable and unstable angina (*A.Celeste, E.Birscic, E.Tessitore, M.Crudelini, A.Alberti, A.Pucci; Turin-I)*

P13 "In vivo" coronary histology and lipid-lowering therapy *(L.Formato, A.Celeste, M.Crudelini, C.Moretti, P.G.Greco-Lucchina, E.Tessitore, I.Sheiban, A.Pucci, G.P.Trevi; Turin-I)*

P14 Pre-clinical trial of a self-xpandable nitinol stent (*M.Prunotto, M.Galloni, S.Gaggianesi, C.Isaia, E.Pasquino; Turin-I)*

P15 Antibody as a possible mediator of apoptotic events in xenograft rejection (*F.Besenzon, M.Seveso, F.Calabrese, G.DeBenedictis, P.Rigotti, E.Cozzi, G.Thiene, E.Ancona; Padua-I)*

P16 Distal protection during carotid artery stenting in symptomatic and asymptomatic patients (*F.Mistrorigo, A.Angelini, B.Reimers, M.DellaBarbera, C.Cernetti, G.Pasquetto, M.Valente, P.Pascotto, G.Thiene; Padua and Mirano-I)*

P17 Contrast-enhanced transthoracic echocardiographic doppler assessment of coronary flow velocity reserve in heart transplant recipients: lack of correlation with acute rejection (*F.Tona, A.L.P.Caforio, A.Angelini, R.Montisci, C.Sarais, A.Gambino, G.Feltrin, M.Ruscazio, A.Vinci, M.G.Leone, G.Gerosa, G.Thiene, S.Iliceto; Padua-I, Cagliari-I)*

P18 The pathology of sudden cardiac death: a specialist centre referral experience (*A.Fabre, M.N.Sheppard; London-UK)*

P19 The histopathology of aortitis of the thoracic aorta and its differential diagnosis with clinico-pathologic correlation (*A.Barbour, M.N.Sheppard; London-UK, Adelaide-AUS)*

P20 Three-dimensional electroanatomic voltage mapping for diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: correlations with endomyocardial biopsy (*L.Leoni, D.Corrado, C.Basso, B.Tokajuk, B.Bauce, A.Ramondo, L.Daliento, A.Nava, G.Buja, S.Iliceto, G.Thiene; Padua-I)*

P21 Concomitant pulmonary venous changes in females with hypertensive pulmonary arteriopathy (*O.Leone, N.Galié, A.Manes, L.Negro, G.G.Pietra; Bologna-I)*

P22 Transmural coronary inflammation "trigger" of instable plaques rupture (*E.Maresi, R.Midulla, E.Orlando, V.Cospite, G.Fazio, R.Porcasi, C.Trapanese, F.Pellegrino, P.Procaccianti; Palermo-I)*

P23 Coronary artery emboli (*S.D.Cohle; Grand Rapids-USA)*

14:30 **Oral communications**
Chairperson: *V. Kanjuh, Belgrade-Y*

O01 Vascular endothelial growth factor gene transfer to mice hindlimb skeletal muscle (*I.Kholova, S.Koota, P.Leppanen, J.Narvainen, S.Yla-Herttuala; Kuopio-FIN)*

O02 3-D reconstruction of fetal heart: a novel approach to fetal cardiopathology (*G.Bussolati, C.Marchiò, M.Volante, A.Grua, G.Botta; Turin- I)*

O03 B-catenin pathway and microsatelite instability status in sarcomas of the pulmonary artery (*A.Gaumann, B.Bode-Lesniewska, D.Zimmermann, F.Hofstadter, W.Dietmaier; Regensburg-D, Zurich-CH)*

O04 Comparison of structure and calcification potential of kangaroo vs porcine aortic valves after glutaraldehyde fixation (*R.G.Forsyth, K.Narine, A.Waeytens, E.Claeys, C.Chery, E.Goethgebeur, M.Praet, G.Van Nooten; Gent-B*)

O05 Histologic determinants of diastolic dysfunction in patients with Fabry cardiomyopathy (*C.Chimenti, M.Pieroni, A.Santagostino, M.A.Russo, A.Maseri, A.Frustaci; Milan-I, Rome-I)*

O06 Fat in the right ventricle of the normal heart (*D.Tanscy, Z.Aly, M.N.Sheppard – London, UK, Harefield-UK)*

16:00 Transfer by bus from Abbey of Praglia to Padua Palazzo del Bo'

17:00 **Opening ceremony and Master lecture - Aula Magna, Palazzo del Bo'**

Address of the Authorities

Chairperson: *G.Thiene, Padua-I*
Therapeutic weapons against atherothrombosis
V. Fuster, New York-USA

18:00 Visit to the Palazzo del Bo'

19:00 Cocktail (Basilica del Bo')

SYMPOSIUM HEART VALVE DISEASE
Chairpersons: P.J. Gallagher, Southampton-UK; L. Daliento, Padua-I

09:00 Surgical anatomy of cardiac valves S07
A. Cook, London-UK

09:20 The current pathology spectrum of valve diseases S08
P. Bruneval, Paris-F

09:40 Clinical non–invasive assessment of heart valve disease: morphological and functional aspects S09
R. Scognamiglio, Padua-I

10:00 Surgical treatment: valve repair S10
O. Alfieri, Milan-I

10:20 Surgical treatment: valve replacement and outcome S11
G. Gerosa, Padua-I

10:40 DISCUSSION

11:10 BREAK

11:30 **Odd cases**
Chairperson: *C.Kirkpatrick-Mainz-D*

O07 An unusual aortic valve (*L.Ffolkes, M.Hayward, D.Brull, S.Krywanych, S.Hughes; London-UK)*

O08 Pelvic "tumor" growing up into right cardiac chambers (*R.Gouveia, M.Abecassis, A.Pina, R.Ribeiras, A.P.Martins; Lisboa-P)*

O09 Arterial changes in gravidic "splenic emergency syndrome" (*A.Marzullo, G.Caruso, G.DiVella, A.Arpaio, M.Colonna; Bari-I)*

O10 Sudden death in a teenager (*D.Phillips; Ashford-UK)*

O11 Claudication in a 44 year old male (*H.Abdelsalam; Stafford-UK*)

O12 Urgent heart transplantation in a 18 year old male (*L.P.Riber-Hansen, U.Baandrup; Aarhus-DK)*

13:00 LUNCH AND VISIT TO POSTERS
Chairperson: *M.J.A.P. Daemen, Maastricht-NL*

P24 Retrieval analysis of mechanical heart valve prostheses: a 30 years experience at a single institution (*T.Bottio, G.Rizzoli, G.Gerosa, G.Thiene; Padua-I)*

P25 Molecular diagnosis of acute myocarditis causing sudden death in young people (*E.Carturan, C.Basso, F.Calabrese, G.Thiene; Padua-I)*

P26 Determinants of heart failure in hypertrophic cardiomyopathy (*F.Bobbo, P.Melacini, A.Angelini, C.Basso, S.Iliceto, G.Thiene; Padua-I)*

P27 Role of magnetic resonance imaging in the arrhythmic risk stratification in repaired tetralogy of Fallot (*G.Russo, A.F.Folino, L.Cacciavillani, F.Corbetti, B.Bauce, L.Daliento; Padua-I)*

P28 Sino-tubular aorta dilatation in aortic valve disease: morphological analysis of medial changes (*S.Esposito, F.Ferraraccio, M.Accardo, P.Santé, M.Cotrufo, L.Cuccurullo, L.Agozzino; Naples-I)*

P29 Desmin-free cardiomyocytes and myocardial dysfunction in end stage heart failure (*S.Esposito, F.Ferraraccio, S.DiSomma, M.P.DiBenedetto, G.Salvatore, G.Caputo, O.DeDivitiis, L.Agozzino; Naples-I, Rome-I)*

P30 Engraftment of extracardiac progenitor cells in an experimental model of heart transplantation (*T.Zaglia, E.Cozzi, A.Dedja, E.Ancona, S.Schiaffino, G.Thiene, S.Ausoni; Padua-I)*

P31 Mutation screening of desmoplakin gene in 40 unrelated Italian index patients with a classical form of arrhythmogenic right ventricular cardiomyopathy (*G.Beffagna, A.Rampazzo, C.Basso, A.Nava, B.Bauce, G.Thiene, G.A.Danieli; Padua-I)*

P32 Mutation screening of SCN5A gene in 35 index patients with Brugada syndrome (*K.Pilichou, A.Rampazzo, S.Baldan, A.Nava, D.Corrado, B.Bauce, G.Frigo, B.Martini, F.Naccarella, C.Basso, G.Thiene, G.A.Danieli; Padua-I, Thiene Vicenza-I, Bologna-I)*

P33 Detection of recipient origin cardiomyocytes in orthotopic heart transplantation (*C.Castellani, A.Angelini, M.DellaBarbera, M.Valente, A.Gambino, A.L.P.Caforio, G.Feltrin, G.Gerosa, G.Thiene; Padua-I)*

P34 V.E.S.A.L.I.O. project (*F.DiMarco, B.Bertipaglia, G.Gerosa; Padua-I)*

P35 Pattern and distribution of fibrosis in the heart of patients dying suddenly of idiopathic cardiac fibrosis (*E.Reed, Y.Ho, M.N.Sheppard; London-UK)*

P36 Myocardial damage with head injury may mimic diffuse myocarditis (*F.MacSweeney, M.N.Sheppard; London-UK)*

P37 Pathology of surgically removed cardiac valves in a specialist UK Center (*M.Gudi, M.N.Sheppard; London-UK)*

P38 New anticalcification treatments of glutaraldehyde fixed bovine pericardium in the subcutaneous rat model (*E.Pettenazzo, G.Thiene, M.Valente; Padua-I)*

P39 Desmosomes in arrhythmogenic right ventricular cardiomyopathy: an ultrastructural investigation of intercalated discs on endomyocardial biopsy (*M.DellaBarbera, C.Basso, M.Valente, E.Wlodarska, B.Bauce, A.Rampazzo, G.Thiene, C.Czarnowska; Padua-I, Warsaw-PL)*

P40 Cardiac amyloidosis – myocardial biopsy diagnosis (*D.Butcovan, C.Arsenescu, C.Borza, D.Pintilie, G.I.M.Georgescu; Iasi-RO)*

P41 Tracheal aspirate a sensitive method for viral detection and tumor necrosis factor alpha in pediatric myocarditis (*Y.Kato, Y.Kato, E.Carturan, F.Calabrese, O.Milanesi, G.Thiene; Padua-I, Toyoake-J)*

P42 Outcome of patients with severe form of arrhythmogenic right ventricular cardiomyopathy/dysplasia (*G.Frigo, B.Bauce, L.Daliento, C.Basso, A.Nava; Padua-I)*

P43 Concealed arrhythmogenic right ventricular cardiomyopathy: pathologic substrates and high resolution MRI (*E.Maresi, L.Russo, R.Midulla, E.Orlando, G.Fazio, A.Pepe, M.Midiri, M.Lombardi, P.Procaccianti; Palermo-I, Pisa-I)*

FRIDAY OCTOBER 22, 2004

14:30 Specimens demonstration and hands-on
C. Frescura, G. Thiene, Padua-I
– Bicuspid aortic valve
–Tricuspid valve disease

16:30 BREAK

17:00 **Key note lecture**
Chairperson: C. Basso, Padua-I
Advances in cardiovascular imaging S12
R. Fattori, Bologna-I

17:30 **Business meeting**

21:00 Congress Dinner (Euganei Hills)

SYMPOSIUM STEM CELLS
Joint Symposium of the Association for European Cardiovascular Pathology and Society for Cardiovascular Pathology
Chairpersons: A.Gittenberger-DeGroot, Leiden-NL; U. Baandrup, Aarhus-DK

09:00 Development of cardiac muscle cell diversity S13
A. Moorman, Amsterdam-NL

09:20 Human and mouse stem cells in repair of the injured heart: functional aspects S14
C. Murry, Seattle-USA

09:40 Endothelial and smooth muscle progenitor cells and their roles in tissue regeneration S15
R.N. Mitchell, Boston-USA

10:00 Factors affecting functional outcome after autologous skeletal myoblast transplantation S16
J-T. Vilquin, Paris-F

10:20 Infarct remodelling after intramyocardial progenitor cell injection treatment in patients with acute myocardial infarction S17
C. Stamm, Rostock-D

10:40 DISCUSSION

11:10 BREAK

11:30 **Oral communications**
Chairperson: M. Burke, Harefield-UK

O13 Juvenile sudden cardiac death: an autoptic analysis (*G.D'Amati, C.R.T.Di Gioia, C.Autore, M.D.Romeo, A.Lopez, C.Ciallella, P.Gallo; Roma- I)*

O14 Clinical-pathological assessment of transplanted human hearts preserved by leukocyte-depleted reperfusion (*L.Dvorak, E.Honsova, J.Pirk; Prague-CZ)*

O15 Overexpression of the glucose regulated protein GRP94 enhances survival of myogenic H9c2 cells transferred into the infarcted myocardium (*L.Gorza, M.Vittadello, M.Crocco, S.Gomirato, F.Zingrino, S.Sponga, G.Gerosa; Padua-I)*

O16 Human CD133 positive stem cells from bone marrow: a good source for therapeutic application (*P.DeCoppi, M.V.Gazzola, R.Destro, A.Angelini, M.Piccoli, F.Castello, E.Slanzi, G.Feltrin, P.G.Gamba, G.Gerosa, G.F.Zanon, C.Messina, L.Zanesco; Padua-I)*

12:30 **Key note lecture**
Chairperson: F. Calabrese, Padua-I
Molecular genetics of sudden death S18
G.A.Danieli, Padua-I

13:00 Closing remarks

ABSTRACTS

S01

S01 Plaques at high risk of myocardial infarction and sudden death

A.C. van der Wal, Amsterdam-NL

Concepts for the pathogenesis of atherosclerotic plaque formation, initiation of atherothrombosis and onset of acute coronary syndromes (unstable angina, acute myocardial infarction and sudden coronary death) have evolved rapidly. In this sequence of events a crucial role for both systemic and local (plaque) inflammation has emerged. And, as a logic consequence, inflammatory parameters are increasingly used as markers for evaluation of disease activity. Numbers of circulating immune cells and their state of activation, serum levels of CRP and other acute phase proteins serve as systemic markers for atherosclerotic disease. Novel imaging techniques aim at detection of plaque inflammation. And moreover, inflammation is now a target for prevention or therapeutic intervention of coronary artery disease (for example the plaque stablizing effects of statins).

In this lecture the specific types of atherosclerotic lesions considered as targets for such new approaches are discussed.

The vulnerable atherosclerotic plaque

These are lesions with a high propensity to develop thrombotic complications or rapid plaque expansion. As such they represent, at least potentially, precursors of unstable plaques. *Vulnerable plaque* is not a single morphologic entity, but over the years distinct variants have been recognized, which probably all differ in the grade of arterial thrombus they may evoke.

1. Rupture prone plaques.

Best studied are the plaques prone to develop deep ruptures that extend into the soft inner parts of lesions. Massive activation of the clotting system readily leads to complete thrombotic occlusion, and ruptured plaques can be found in many cases of transmural myocardial infarction or sudden coronary death. Several distinct morphological and biomechanical features have been identified in ruptured plaques, which are alltogether:

- active inflammation in the fibrous cap orchestrated by activated T-cells, (foamcell type) macrophages and mastcells
- a thin fibrous cap in which high circumferential wall stresses occur
- a large and soft core of extracellular lipids (>40% of plaque volume)
- paucity of smooth muscle cells due to senescence or (cytokine induced) apoptosis, and low collagen content

Rupture prone plaques account for circa 60-70% of all cases of MI or sudden death.

2. Erosion prone plaques.

In another 30-40% of culprit plaques, the thrombus overlies a largely intact plaque that is in part denuded of endothelium or lined with dysfunctional endothelium. Most if not all eroded plaques have at least some degree of inflammatory activity, either throughout the lesion or in other cases as superficially located infiltrates. Rims of foamcell macrophages admixed with lymphocytes, closely apposed to the overlying thrombus and sometimes only a few cell layers thick, can be found regularly in such

lesions. Recently we identified inflammatory "erosion prone" areas in 22% of 115 angiographically detected plaques in the coronary system of 8 patients with coronary artery disease at autopsy. Moreover, 4% of lesions showed erosion and thrombus on the top of the inflammatory lesion. Such observations also support a view of multifocal or pan-coronary vulnerabilty as has been forwarded by specialists from several disciplines. Thrombus formation is often not so dramatic as in ruptured plaques. In most cases they form a substrate for mural thrombus, but in high grade stenotic lesions plaque erosions may also lead to comlete thrombotic obstruction. Moreover, they may serve as a source of coronary micro-embolization.

3. Calcified nodules.

A probably rare cause acute coronary complication recognized by others is the so called calcified nodule which extends with rigid and sharp outlines into the lumen of the artery and may thus increase thrombogenicity of the lesion.

4. Intraplaque haematoma.

Last but not least, there is at present much interest for plaque microvessels in the genesis of clinically manifest coronary disease. Rupture of these capillary or venular sized microvessels cause haematomas inside the plaque, which in turn may lead to rapid expansion of plaque volume and stenosis rate. Also here, inflammatory infiltrates are almost invariably found in the proximity of microvessels and could induce leakiness of vessels. Plaque haematomas, either fresh (indicated by erythrocyte extravasztions) or old (indicated by Glycophorin A stainable erythrocyte remnants, siderophages and / or foci of young collagen) can be observed regularly in culprit- and also non culprit lesions at autopsy.

Coronary thrombosis and the onset of clinical events

Acute coronary syndromes cannot be explained simply by the presence of thrombus on the top of a plaque. In fact, symptomatic coronary artery disease is the (unlucky) result from interaction between processes inside and outside the coronary plaque.

Briefly, plaque features as discussed above determine the vulnerability of a plaque to disrupt, erode or develop plaque haematoma; The time of onset of an acute complication depends on rupture triggers, such as vasospasms, elevated blood pressure, catecholamine releases and others. The final outcome of such events ranges from only a minute thrombus that remains clinically unnoticed, to mural thrombus or even complete thrombotic occlusion. This in turn depends on other variables, such as pre-existent rate of stenosis, the extend of plaque laceration and most important: the thrombotic state of the patient. In other words, the onset of acute coronary artery disease depends on a trias of 'vulnerable plaque', 'vulnerable blood' and 'vulnerable patient'.

Notes:

S02

S02 Triggers and clinical markers of acute coronary syndromes

F. Crea, Roma-I

It is well recognised that atherogenic stimuli like hypertension, hypercholesterolemia, smoking and diabetes cause endothelial dysfunction followed by chemo-attraction of inflammatory cells which then migrate in the subendothelium and originate the atherosclerotic plaque. It is likely that both the intensity of atherogenic stimuli and the reactivity of inflammatory cells play a key role in the transition from endothelial dysfunction to plaque formation. This contention is supported by the observation that in asymptomatic subjects long-term risk of major cardiovascular events conferred by raised serum levels of C-reactive protein (CRP), a prototypic marker of inflammation, and by the presence of traditional risk factors is additive. Furthermore, an inflammatory outburst, with activation of both innate and adaptive immunity[1], plays a key role in the sudden transition from the asymptomatic or stable phase of coronary atheroscleorsis to acute coronary syndromes. Cytokines released by activated inflammatory cells in the culprit stenosis have the potential to cause endothelial activation, plaque fissuring and vasoconstriction. Although the triggers of this inflammatory outburst are still speculative, recent observations suggest the intriguing possibility that inflammation is widespread in the whole coronary circulation[2,3] and extends into the myocardium[4], thus suggesting that "focal" treatment of the culprit stenosis might be insufficient to improve prognosis. Accordingly, the intensity of inflammation, as assessed by measuring serum levels of C-reactive protein (CRP), a prototypic marker of inflammation, predicts an adverse outcome even in patients submitted to an early invasive strategy. Of note, in patients with acute coronary syndromes troponin (Tn), CRP and B-type natriuretic peptide (BNP) provide incremental prognostic information. Indeed, Tn is likely to be a marker of thrombotic burden, CRP appears to reflect the persistence of destabilising stimuli and BNP is a marker of hemodynamic stress. Thus, a simple multimarker strategy that categorizes patients based on the number of elevated biomarkers at presentation might allow risk stratification over a broad range of short- and long-term major cardiac events. Finally, CRP is a marker of the "iatrogenic" inflammation caused by stent implantation. In this setting also, CRP predicts restenosis both in stable and unstable patients. Prospective studies are warranted in order to establish whether the prognostic information conveyed by CRP may improve treatment targeting in primary and secondary prevention of ischemic heart disease and after percutaneous coronary interventions[5].

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Notes:

S03

S03 In vivo detection of vulnerable plaque: invasive imaging

R. De Caterina, Chieti-I

The *in vivo* detection of plaque characteristics associated with vulnerability has made tremendous progress in these last years. Invasive techniques, going beyond morphological features of the lumen contour, as detectable by angiography, now include the following:

- intravascular ultrasounds;
- optical coherence tomography;
- thermography
- virtual histology
- infrared spectroscopy
- IVUS elastography
- intravascular Magnetic Resonance Imaging (MRI)

The principles underlying each of these techniques will be illustrated and limitations as well as areas of complementarity highlighted. New imagining techniques promise to define the anatomical characteristics of coronary plaque prone to rupture. These invasive techinques, in conjunction with recently developed assays, non-invasive imaging and future genomic techniques, will likely guide future cardiologists in the search for lesions to tackle specifically and/or of vulnerable patients.

Notes:

S04

S04 In vivo detection of vulnerable plaque: non invasive imaging

J. Narula, Orange-USA

It is expected that coronary artery disease will continue to be the leading cause of morbidity and death in this century, both in men and women, and in developing and developed nations alike. The management of coronary artery disease has almost always been based on demonstration of the severity of luminal stenosis. Such an approach does not characterize the plaque morphology that happens to be the major determinant of clinical outcome. Limited success has been achieved by the use of angioscopy and intravascular ultrasonography or more recently with optical coherence tomography. All these techniques are invasive and have limited depth resolution. Appropriate targeting strategies with radionuclide imaging techniques could identify the predominant cellular population in the atherosclerotic plaque and help predict the likelihood of clinical events. For an achievement of high target-to-background ratio in radionuclide imaging, it is important to identify the morphologic characteristics of the lesion that are uniquely expressed during the evolution of atherosclerotic process (hot-spot imaging) or those that are selectively deleted from the affected area (cold-spot imaging).

Development of atherosclerotic lesions is an immunoinflammatory response of the intima to injury and involves a complex interplay of components of blood vessels wall with blood elements. The injury is initiated by oxidatively modified lipids that permeate through the endothelial layer. A concurrent expression of selectins and adhesion molecules on the endothelium leads to recruitment of monocytes and their subendothelial migration. The altered release of vasoactive substances from the endothelium facilities phenotypic alteration of medial smooth muscle cells. At this time, the interaction of endothelial cells, adherent monocytes, and modified lipids leads to release of growth factors that induce proliferation or phenotypically altered smooth muscle cells and eventually their migration to the intima. Monocytes and smooth muscle cells in the subendothelial space ingest modified low-density lipoprotein (LDL) cholesterol and evolve into foam cells. The modified lipid uptake in the monocytes occur through non-classical LDL scavenger receptors and is not inhibited by the intracellular lipid. Foam cells are restricted from moving away from the lipid core. Any one of the three major constituents of the plaque, namely lipids, inflammatory cells, and proliferating muscle cells, can be targeted with radiolabeled agents for noninvasive detection of the lesion.

Fourteen million people in the United States have coronary artery disease. Although recognition of each one of them may constitute the ideal situation, it should be most desirable to identify a subset of patients with likely development of acute coronary event. Of the 14 million, 1 million people have development of acute coronary event, and 400,000 die of that event every year. It is now well recognized that progressive luminal stenosis of the coronary artery is often not associated with an acute event and that the tromobotic occlusion usually occurs as a result of plaque rupture. The plaques that are vulnerable to rupture have large lipid cores, attenuated fibrous cap, and

intensed infiltration of macrophages. It has been proposed that the macrophages release metalloproteinases that digest matrix and induce fibrous cap rupture. The plaque rupture exposes thrombogenic lipid core leading to thrombotic luminal obstruction. Therefore for the identification of vulnerable plaques, morphologic techniques such as IVUS, MRI, OCT and CT have capitalized on attenuated fibrous caps and large lipid cores. Nuclear imaging can be best exploited for localization of macrophage infiltration in the atherosclerotic plaque. It is conceivable that only those macrophage antigens should be targeted that are expressed on the resident macrophages and not borne by the circulating monocytes.

Notes:

S05

S05 Interventional treatment of acute coronary syndromes

B.Reimers, Mirano Venice-I

Introduction. Embolization of thrombus and plaque debris during primary angioplasty for acute myocardial infarction (AMI) may lead to distal vessel or side branch occlusion and to obstructions of the microvascular system, causing no-reflow and suboptimal tissue reperfusion. Mechanical intracoronary thrombectomy (MIT) is thought to reduce macro and micro embolization of debris, potentially improving myocardial reperfusion. In recent years, several studies aiming to evaluate the effects on myocardial reperfusion of mechanical thrombectomy in the setting of direct angioplasty for acute myocardial infarction (AMI) have been carried out.

Methods and Results. Three ramdomized studies compared the use on the X-Sizer thrombectomy device *vs* conventional primary angioplasty in patients with AMI (1-3). The first monocentric study, carried out by Beran et al, demonstrated that x-sizer ameliorates correct TIMI frame count and ST-segment resolution respect to conventional primary angioplasty (1). The second monocentric study, performed by Mirano Group, showed that MIT with X-sizer increases the incidence of final Blush 3 grade at angiography anf of ST-segment resolution at post angioplasty EKG (two parameters indicating the achievement of a good myocardial reperfusion), and reduces the incidence of angiographic complications related to dislodgment of thrombus like no-reflow, macroscopic distal embolization and side branch occlusion (2). The third multicenter study, demonstrated that X-sizer increases the incidence ST-segment resolution and decrease the incidence of angiographic complications (3).

Three studies evaluated the use of the AngioJet thrombectomy device *vs* conventional primary angioplasty (4-6). Two monocentric, non-randomized studies demonstrated a benefit with the use of the AngioJet in term of a better final TIMI flow in the infarct related artery; one (5) of them found also a better ST-segment resolution at post angioplasty EKG and a higher left ventricular ejection fraction at follow up. In the only prospective, multicenter, randomized study comparing Angiojet thrombectomy *vs* primary angioplasty (6), the use of Angiojet was associated with worse prognosis in terms of infarct size and in-hospital mortality.

Conclusion: The results of preliminar studies evaluating intracoronary thrombectomy as adjunct to stenting during direct angioplasty for AMI are incouraging but not still conclusive.

Further studies are needed to definitively demonstrate the benefits of such approach and to identify the more efficacious thrombectomy device.

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Notes:

S06

S06 Experimental Atherogenesis

H-A. Lehr, Mainz-D

Atherosclerosis is a human disease that is characterized by a slow, insidious affection of medium sized and large muscular arteries that provides the morphological basis for gradual vessel obliteration (resulting in clinical phenomena like intermittent claudication and angina pectoris) and vessel occlusion secondary to plaque ruptur and thrombosis (resulting in such dramatic events like stroke and myocardial or mesenteric infarction). Abundant information has accumulated regarding risk factors (i.e. hyperlipidemia, smoking, etc.) and preventive strategies (i.e. physical exercise, etc.) that affect the progression of atherosclerosis and it's clinical sequelae in humans. Yet, the exact mechanisms of atherogenesis are still open to vivid debate and formulated in mere hypotheses such as the „oxidative hypothesis", the „respose to injury hyothesis" or the more recent „Mainz hypothesis" that postulates a pivotal role of enzymatically modified LDL (rather than oxidatively modified LDL) and complement in atherogenesis.

Animal models have been developed to mimic as closely as possible the morphological consequences of atherogenesis and it's pathogenesis. A brief overview over the history of experimental atherogenesis is given, starting at the turn of the last century when rabbits were hung up by their hind legs to induce a type of „atherosclerosis", over the use of fowl, dogs, pigs, non-human primates and eventually the generation of transgenic mice that until only a few decades ago had been considered entirely unsuitable for atherosclerosis studies in their respective wild types. The methodology atherosclerosis quantification in aortic valve cusps, the aortic surface (*en face*) and large branching vessels is presented using examples from my own laboratory, along with some recent, partially unpublished findings on the role of the innate immune system, of reactive oxygen species, and of C-reactive protein in experimental atherogenesis in rabbits and mice.

Even though in all these animal models, lesions are rapidly generated (within weeks to months) through cholesterol feeding or through genetic manipulations (usually affecting the cholesterol metabolism), it will become quite clear from my presentation that none of the presently available animal models adequately reflects the pathophysiology and/or the morphology of human atherogenesis. Either the lesions do not look right (i.e. the pure foam cell lesions in hypercholesterolemic rabbits and LDL-R deficient mice) or the animals are deficient/defective in key pathomechanisms that are relevant in human atherogenesis (i.e. ApoE knock-out mice lack a functional complement system). Some animals exhibit a lipoprotein system that is diametrically different from it's human counterpart (in mice, cholesterol is transported in HDL and not in LDL). Despite excessive inbreeding and well characterized genetic manipulations, atherogenesis differs tremendously from animal to animal both between laboratories (resulting in conflicting findings in the literature, e.g. the antiatherogenic effect of vitamin E in ApoE knock-out mice) and even within the same laboratory (requiring large numbers of animals per experimental group). Also, trivial

details of animal husbandry have to be taken into careful consideration, such as the supplementation of antioxidant vitamins in animal diets). Finally, none of the present animal models is suitable to model plaque rupture, the event that is of prime importance for atherosclerosis-related morbidity and mortality in humans.

Notes:

S07

S07 Surgical anatomy of cardiac valves

A. Cook, London-UK

The normal heart possesses atrioventricular and ventriculo-arterial junctions, and these are guarded by atrioventricular and arterial valves, respectively. Each set of valves has various component parts that form a valvar 'complex' which must all work in harmony so as to ensure valvar competence.

The atrioventricular valves possess an annulus, leaflets, tension apparatus and papillary muscles. It is often though that the annuluses are complete fibrous rings which are part of the "fibrous skeleton". This can be the case for the mitral valve, but particularly in the tricuspid valvar orifice, the leaflets are hinged at the fibrofatty tissue of the atrioventricular junction. It is the leaflets which are the "working parts" of the valvar apparatus. There is controversy as to the best method of distinguishing between the extent of the leaflets. Examination of the atrioventricular valves in their closed position, nonetheless, makes it an easy matter to distinguish two leaflets in the mitral valve and three in the tricuspid valve. The two leaflets in the mitral valve occupy aortic, or anterior, and mural, or posterior, positions within the left atrioventricular junction. The aortic leaflet, is in fibrous continuity with two of the leaflets of the aortic valve. The tricuspid valve possesses leaflets disposed in septal, antero-superior, and inferior, or mural, position.

The tension apparatus of the valves is arranged so as to give uniform support to the free-edges of the valvar leaflets. Complex definitions have been provided for the various orders of tendinous cords. It is sufficient to define free-edge cords, cords running to the rough zones, and basal cords. The papillary muscles are usually positioned so as to support the tension apparatus beneath the junctions between the leaflets. An important feature of the tricuspid valve is the multiple tendinous cords attached directly to the septum, a feature which is lacking in the normal mitral valve.

Just as the leaflets are the major "working parts" of the atrioventricular valves, so they are the most important constituents of the arterial valves. The feature of the arterial valves is that their leaflets do not possess tension apparatus. The main anatomic feature of the arterial valves, therefore, is the semilunar nature of the attachment of the leaflets within the arterial root. Normal arterial valves possess three leaflets, which close together in trifoliate fashion. The peripheral attachment of the zones of apposition between the leaflets is at the sinutubular junction of the arterial trunk. The basal attachment of each semilunar leaflet is then within the ventricular outflow tract. As the semilunar attachments of the leaflets extend from the sinutubular to the basal points, they cross over the anatomic ventriculo-arterial junction. This intricate arrangement then produces an interdigitation of sinuses and interleaflet triangles, an appreciation of which is important in understanding the mechanisms of valvar function. The pulmonary valvar has its leaflets supported exclusively by the free-standing muscular subpulmonary infundibulum. The situation is different for the aortic valve. Here, it is only the two sinuses which give rise to the coronary arteries which arise from the musculature of the ventricular septum. The non-coronary aortic sinus is supported by the aortic leaflet of the mitral valve.

S08

S08 The current pathology spectrum of valve disease

P. Bruneval, Paris-F

Cardiac valve pathology has changed during the last ten years because the etiologies and the surgical treatment of valve diseases have also changed. For these reasons, pathological examination and diagnosis require adaptations from old classical valve pathology.

New conditions of cardiac valve sampling: Valve repair is now the gold standard treatment at least for mitral valves in most patients treated in our countries: the corollary of that is that the pathologists now have at their disposal only a part of the valve apparatus to examine. Accurate description and adequate technical preparation (including systematic histological examination) of that size of valve samples are essential for pathological diagnosis.

Changes in etiologies of valve diseases: Degenerative valve diseases

They are now the most frequent cause of valve diseases mainly for the mitral valve where they account for most if not all cases of primary mitral valve incompetence's. They are called by different names "Barlow's disease", "mitral valve prolapse", "myxoid degenerative changes". Gross and microscopic pathology are characterized by some variations resulting in the different names. However, common patterns observed in degenerative mitral incompetence are: increased length of the mitral ring (treated with prosthetic ring), excessive abundant mitral valve tissue (allowing surgical repair using wedge resection), some degree of fibrosis, some degree of myxoid tissue overload, and severe alterations of elastic fibers; Endocarditis: Although powerful antibiotics are now available, endocarditis is still a severe disease leading to valve replacement or repair because of highly virulent germs inducing rapidly devastating lesions in cardiac valves. In case of blood culture negative endocarditis (previous antibiotic inadequate treatment or fastidious bacteria), the role of the pathologist is crucial to ensure the diagnosis of endocarditis based on inflammation and careful detection of bacteria within the inflammation by using special stains and immunofluorescence; The antiphospho-lipid syndrome: Among the systemic diseases involving the cardiac valves, a newly recognized one is the antiphospholipid syndrome. As for arterial manifestations, thrombosis is the main feature. It is responsible for non-infectious vegetations mainly on mitral valves. Known for many years as Libman-Sacks endocarditis in systemic lupus, they are in fact related to antiphospholipid antibodies and are observed in lupus as well as in primary antiphospholipid syndrome; The cryopreserved valve homografts are an alternative material to valve prosthesis when valve replacement is required. The are submitted to degenerative processes and probably chronic rejection.

Notes:

S09 Clinical non–invasive assessment of heart valve disease: morphological and functional aspects

R. Scognamiglio, Padua-I

The goal is to discuss succinctly the advanced state in diagnosis and treatment of VHD.
In 1950, rheumatic valvular heart disease (VHD) was the most common cause of VHD. The link between streptococcal infection and rheumatic fever was established, and a successful trial of penicillin prophylaxis against rheumatic fever was reported. It was well recognized that the mitral valve was the valve most commonly affected in rheumatic heart disease. As a consequence, closed-chest mitral commissurotomy for mitral stenosis was the most common early and successful cardiac surgical intervention. 1960 was the start of heart valve replacement. Two major classes of valves are: (1) mechanical prosthetic valves and (2) biological (tissue) valves, which include autograft, homograft (allograft), and bioprosthesis (xenograft). Mechanical heart valves were first used in 1960 by Harken, and Starr and Edwards. By the mid-1970s, it was recognized that the major clinical problem with mechanical valves was thromboembolism and that with bioprostheses was limited durability because of valve degeneration.
The use of high-frequency ultrasound to assess cardiac structure and function is one of the great advances in the past 50 years. It has greatly enhanced our ability to safely and accurately make cardiac diagnoses. Echocardiography allowed noninvasive hemodynamic assessment of VHD which optimized surgical timing in VHD with a chronically overloaded left ventricle. Other examples of important applications of ecocardiography include: 1) monitoring of vegetations and metastatic events in infective endocarditis, 2) assessment of contractile reserve as indicator of surgical correction in patients with low gradient aortic stenosis and LV dysfunction. Serial noninvasive evaluations of LV function in patients with chronic LV overload allowed to obtain new insights on the clinical and pathophysiological understanding of these patients: in chronic severe aortic regurgitation, it has been demonstrated that not all patient require aortic valve replacement and that a vasodilator therapy can reduce or delay the needs for surgical correction; in the setting of patients with mitral regurgitation, emerging evidences indicate a possible role of factors different from hemodynamic overload in conditioning the progression of the disease: correction of the LV volume overload with MV surgery results in reversal of TNF- expression. There is a relationship between TNF- expression and parameters of LV remodeling, suggesting that TNF- may play a role in the pathogenesis of the LV remodeling that occurs in MR.
Finally, of great clinical and pathophysiological interest are the studies analyzing the mechanisms of coronary microcirculatory dysfunction in the presence of marked increase of LV mass in patients with aortic stenosis and angiographically normal coronary arteries: some studies indicate that development of LV hypertrophy in aortic stenosis accompanied by coronary microcirculatory dysfunction, demonstrated by an impaired coronary vasodilator reserve (CVR). CVR was more severely impaired in the subendocardium, and the severity of impairment was related to aortic valve area, hemodynamic load imposed, and diastolic perfusion rather than to LVM.

S10 Surgical treatment: valve repair

O. Alfieri, Milan-I

Valve repair is preferable to valve replacement since it is associated with higher survival,lower complication rate and better quality of life.
Pure mitral regurgitation can be treated with mitral repair in more than 90% of the cases, regardless the mechanism and the etiology. Long term survival is similar to that of the general population matched for age and sex, if the operation is carried out before the occurrence of left ventricular dysfunction.
Annuloplasty, leaflet resection, implantation of artificial chordae,chordal transfer and edge to edge repair are some of the techniques more frequently used to correct specific lesions.
The feasibility of the repair, the type of the repair and the results can be easily predictable by preoperative echocardiography.
Patients with rheumatic disease, in whom both mitral stenosis and insufficiency are present, are less likely to be amenable to valve repair, particularly in presence of calcified leaflets.
On the contrary, functional mitral regurgitation, as seen in patients with ischemic or idiopatic dilated cardiomyopathy, can be often successfully treated with an undersized annuloplasty.
Repair of the aortic valve is recently carried out in selected patients. When the aortic valve is morphologically normal but incompetent due to annulo-aortic ectasia,a valve sparing operation can be performed. Also cusp prolapse can be effetively corrected, plicating the redundant free edge.
Pericardial cusp extension to correct cusp retraction is associated with less predictable and gratifying results.
The use of 3-D echocardiography has a major role in detecting candidates for aortic valve repair.

Notes:

S11

S11 Surgical treatment: valve replacement and outcome

G. Gerosa, Padua-I

The modern era of valve replacement started in 1960 when Dr. Dwight Harken successfully replaced an aortic valve. On the same year, Starr and Edwards performed the first mitral valve replacement procedure. A caged-ball was adopted in both cases. In 1964 the first xenograft porcine aortic valve was implanted in aortic position by Duran and Gunning.

Forty years after the beginning of the prostheses' era, the choice of the most proper valve substitute is still challenging. Bioprostheses and mechanical valves are still the main characters, but during the last decades many factors have been modifying the pattern of valvular surgery.

1) Patients' profile: because of the improved longevity and quality of life, life-expectancy has increased. Aortic stenosis is now the most common adult valvular disease in the western countries, reaching a prevalence of 4% in patients over 85 years.
2) Prostheses' durability: current bioprostheses evidenced a longer durability expecially in older patients
3) Prostheses' thrombogenicity: modern mechanical prostheses are characterized by a reduced thrombogenicity requiring a lower dosage of anticoagulants. Furthermore, the anticoagulant management and surveillance contribute to minimize the risk of major hemorrhagic events.
4) Outcome: octogenarians show higher rates of operative mortality (5-15% for aortic valve replacement). On the other hand, the gain in terms of prognosis and long-term survival after valve replacement is comparable to younger patients (5-year survival 55-70% for AVR)

Operative outcome and long–term survival are also influenced by other factors on which both cardiac surgeons and cardiologists can act during the decision making process: coexisting commorbidities often accompanying advanced age which must be throrougly investigated and post-operative long-term secondary cardiac–failure whose progress can be avoided by an early operation.

Finally the new alternative valve substitutes offered by the emerging tissue engineering technologies will potentially amplify cardiac surgeons options.

Notes:

S12

S12 Advances in cardiovascular imaging

R. Fattori, Bologna-I

In the past few years advances in technology have lead to total revolution in diagnostic imaging. Important recent developments have occurred in echocardiography. Portable ultrasound devices that weigh less than five pounds are capable of performing a complete bedside exam. The use of contrast media, the evolution of 3D technique and tissue doppler imaging, provided potential impact to improve the assessment of both morphologic and functional parameters of cardiovascular system. Cardiac positron emission tomography (PET) is widely regarded as a "gold" standard in the assessment of myocardial viability. Improvements in spatial resolution and the development of new tracers have made also possible its application to perfusion imaging, coronary flow reserve, plaque and molecular imaging.

Remarkable advances in non invasive imaging techniques, notably computed tomography (CT) and Magnetic Resonance(MR) imaging have replaced many invasive procedures, lowering the costs and morbidity of diagnosis. Multidetector CT represented a breakthrough in CT technology. It has transformed CT from an transaxial cross-sectional technique into a true 3D imaging modality that allows for arbitrary cut planes as well as excellent 3D displays of the data volume. In less than 4 years CT coronary angiography has improved from 81% to 94% its sensitivity in the detection of coronary artery stenosis. Increased scan speed with retrospective gating allows coverage of the entire cardiac volume with 1-mm collimated slice widths in one breath hold. Initial results from studies in correlation with intracoronary ultrasound suggest that MDTC technology not only offers the possibility to visualize intracoronary stenoses non-invasively but also to differentiate plaque morphology. Rapid progress has been made in cardiac MRI over the past decade which has firmly established it is a reliable and clinically important technique for the assessment of cardiac structure, function, perfusion and myocardial viability. Its versatility and accuracy is unmatched by any other imaging modality. CMRI is non-invasive avoiding the use of nephrotoxic contrast agent and radiations, therefore it may represent the method of choice in complex follow-up examinations such as in congenital heart diseases. The possibility of tissue characterization may improve the diagnostic capability in the evaluation of cardiac masses or cardiomyopathies as well as in the assessment of ischemic heart diseases. Continued technological progress promises to further widen its clinical applications in coronary imaging, myocardial function and perfusion and vascular assessment. Published diagnostic validation studies, convenience, procedure time, comfort level (of patients and physicians), availability, and cost are all critical in the difficult choice among excellent imaging modalities. However, considering the high technological characteristics and continuous growth, we should expect in the next future a progressive leading role of MRI and CT in the diagnosis of heart disease.

S13 Development of cardiac muscle cell diversity

A. Moorman, Amsterdam-NL

In Western populations the incidence of heart failure increases due to aging of the population and increasing survival rates after myocardial infarction. The remaining cardiac muscle is forced to take over the task of the part that was lost due to the infarction. Fundamental in our understanding is to know the options and the limitations not only of the remaining cardiac muscle cells but also of the cardiac fibrous tissues.

The heart has a mesodermal origin with a minor contribution of neural crest cells. Commitment of mesodermal cells to the cardiogenic lineage is established during and shortly after gastrulation. The three principal cardiac cell types comprise *1.* the endocardium that forms the endothelial lining of the heart, *2.* the myocardium or cardiac muscle cells, and *3.* the epicardium that is the source of cardiac fibroblasts and coronary arteries. The three tissue types share a common lineage and experimentally, both the endocardium and the (pro)epicardium are able to trans-differentiate into cardiac muscle cells. The myocardium-forming potency of the endocardial and pro-epicardial cells *in vitro* indicates that they are not irreversibly committed to endocardial or epicardial lineage, respectively. These observations are of great clinical interest, because the endocardium and particularly the epicardium are the most important source for cardiac fibroblasts.

A rational therapeutic therapy of failing hearts requires not only profound knowledge of these processes but also of the mechanisms that underlie the unique patterns of expression in the different regions of the heart, in order to achieve activation of the therapeutic gene at the proper place. We have found that regions in the embryonic heart that hardly proliferate and will not develop into atrial or ventricular chamber myocardium do express the transcriptional repressor Tbx2 and Tbx3. These factors are able to repress *in vitro* transcriptional activity of the Nppa (ANF) promoter, which is a marker for chamber myocardium. In the regions that express Tbx2 or Tbx3, the cardiac conduction will develop. For the first time we have a clue about the mechanisms that determine the specification of the distinct cardiac muscle cells.

Notes:

S14 Human and mouse stem cells in repair of the injured heart: functional aspects

C. Murry, Seattle-USA

The heart has a very limited regenerative capacity, and consequently, myocardial infarcts heal by scar formation. Over the last 10 years, our group has been interested in cell-based approaches to repair the infarcted heart. Difficulties in identifying sources of differentiated human cardiac myocytes have led us to focus on stem cells. We found that direct injection of hematopoietic stem cells did not form new myocardium in infarcts in mice. Bone marrow transplants with EGFP-tagged marrow revealed that a few cardiomyocytes arose from endogenous marrow cells after infarction, but the very low frequency (<0.01%) was most consistent with fusion rather than transdifferentiation. Analysis of human heart transplants, where female hearts were placed in male recipients, showed that rare cardiomyocytes (~0.04%) arose from extracardiac progenitors. In contrast, ~25% of endothelial cells, ~11% of perineural Schwann cells, and ~3% of coronary arterial smooth muscle cells arose from extracardiac sources. These findings indicate that most cell types in the heart can arise from extracardiac sources, but the frequency varies widely by cell type. Adult stem cells seem plausible candidates for vascular regeneration, but cardiomyocyte regeneration is at best very inefficient.

In contrast to adult stem cells, embryonic stem cells (ESCs) have unquestioned plasticity and are well known to generate cardiac myocytes. In collaboration with Geron Corp., we have initiated a program in human ESCs for cardiac repair. Unlike mouse or rat cells, human cardiomyocytes derived from ESCs have a high proliferative capacity in vitro. This proliferation is only modestly serum-dependent, suggesting an autocrine/paracrine pathway. We found that proliferation could be blocked by small molecule antagonists of PI3-kinase or Akt, but not through inhibition of MAP kinase. Furthermore, addition of IGF-1 or –2 stimulate proliferation of human cardiomyocytes, whereas IGF-1 receptor blockade inhibited their basal proliferation. These data suggest an autocrine/paracrine loop whereby IGF-1/2 produced by these cultures stimulate the IGF-1 receptor and activate PI3-kinase and Akt pathways downstream. Finally, we have recently found that human cardiomyocytes can form stable grafts of human myocardium when implanted into the hearts of nude rats. The human myocardium expressed features characteristic of fetal myocardium (high glycogen content, expression of ANF, b-myosin heavy chain, MLC-2v, sarcomeric actin etc.). Furthermore, these grafts proliferated significantly, with 6.4% and 2.7% incorporating BrdU at 1 and 4 weeks post-transplantation, respectively. Recent studies indicate that human myocardium also can be formed in infarcted rat hearts by cell transplantation. This system should permit studies of human myocardial development and provides support for the eventual use of these cells in cardiac repair.

Notes:

S15

S15 Endothelial and smooth muscle progenitor cells and their roles in tissue regeneration

R.N. Mitchell, Boston-USA

Recent reports of bone marrow-derived and cardiac intrinsic stem cells offer exciting therapeutic possibilities for repopulating the myocardium, previously considered a terminally differentiated tissue incapable of any significant regeneration or repair. Concurrently, there is a growing appreciation that similar populations of stem cells also contribute to a host of vascular pathologies. Thus, circulating host-derived precursors are the major contributors to the concentric intimal hyperplasia of smooth muscle-like cells that progressively compromise the circulation of solid organ allografts (transplant-associated arteriopathy). Moreover, the same precursor populations may also bring about the vascular stenoses that occur following a variety of vessel wall injury: balloon and stent restenosis, stenoses associated with bypass anastomoses, and even atherosclerosis. The presentation will highlight the experimental animal data and human findings from the organ transplantation experience and discuss the origin of vessel wall precursors as well as potentially unique pathways by which these cells access sites of vascular injury.

Notes:

S16

S16 Factors affecting functional outcome after autologous skeletal myoblast transplantation.

J-T. Vilquin, Paris-F

Post-ischemic heart failure becomes a major issue for public health, and therapeutical options are limited. Therefore, muscle cell transplantations were developed as alternative strategies to improve cardiac structure and function. While adult cardiomyocytes lack the abilty of self-renewal, the aptitude of skeletal muscle cells (SMC) to repopulate healthy or infarcted myocardium has been investigated in numerous animal models. The transplantation of SMC in the infarcted area leads to increased myocardial function in correlation with the development of skeletal muscle tissue (myoblasts, myotubes, muscle fibers). The functional benefit is related to the number of injected cells, but its mechanisms are not understood yet. Intracellular recordings coupled to video and fluorescence microscopy established that the newly formed tissue retained excitable and contractile properties, which remained fully independent of neighboring cardiomyocytes. No direct coupling could be demonstrated, nor transdifferentiation of SMC towards a cardiomyocyte lineage. The functional benefit persited over more than one year in Rats and Sheeps, despite a decline in number of skeletal muscle structures with time.

The GMP scale-up of human cell production was completed in agreement with the French Health authorities and the first phase I clinical trial (feasibility, safety) for intramyocardial autologous myoblast transplantation was performed in 2000-2001. At the same time the 10 patients received a coronary bypass surgery, they were injected with 500 million to 1.1 billion autologous cells in a non-viable, non-revascularisable infarcted area. Postoperative, monthly repeated echographies showed an increased systolic shortening in the previously akinetic injected area. PET scan data revealed a new-onset metabolic activity in this area. The ejection fraction improved, although it is difficult to attribute the improvement to bypass, or to cell transplantation. Four patients presented delayed and transient ventricular tachycardia events and received an automatic defibrilator and transient anti-arrythmic treatment. The origin of the arrythmia is not known, since these events are not rare in patients suffering from heart failure. Given the encouraging results, the MAGIC trial (Myoblast Autologous Grafting in Ischemic Cardiopathy) has been set up to evaluate the efficacy of the approach. This is a randomized, international muticentric phase II clinical study in which 300 patients will be included.

The researches are now extended toward non-ischemic dilated cardiomyopathies through the use of the CHF147 Syrian Hamster, a strain characterized by a delta-sarcoglycan deficiency which phenotypically features the human setting of primary dilated cardiomyopathy. Following autologous SMC transplantation, an improvement of function was observed, in parallel with the development of skeletal muscle tissue. Further researches are developed to understand the fate of injected cells, and to improve their survival, proliferation, implantation.

Finally, the cell production plateform is also used to evaluate the usefulness of myoblasts in other clinical fields, such as muscular dystrophies.

S17

S17 Infarct remodelling after intramyocardial progenitor cell injection treatment in patients with acute myocardial infarction

C. Stamm, Rostock-D

Cardiovascular diseases, especially ischemic heart disease, remain the No. 1 cause of death in industrialized countries. When preventive measures fail and myocardial infarction occurs, myocardium is subject to – supposedly - irreversible necrosis. Because the consequences are often hazardous, strategies for regeneration of necrotic myocardium are under intensive investigation. One of the most promising approaches is the implantation of progenitor cells or pluripotent stem cells in infarcted myocardium. The ability of bone marrow-derived adult stem cells to trans-differentiate into cells of various target-organ phenotypes is a matter of current and very controversial discussion. While accumulating evidence obtained in a variety of experimental models as well as clinical pilot studies clearly indicates that adult stem cells can indeed improve heart function after myocardial infarction, the cellular mechanism remains unclear. The initial euphoria regarding the capacity of unmodified bone marrow or blood-derived stem cells to trans-differentiate into cells of cardiomyocyte phenotype has faded. A beneficial impact on angiogenic processes in ischemic tissue is more consistently observed, but it remains controversial whether this reflects true stem cell trans-differentiation along the angiogenesis axis, growth factor and cytokine release by stem cells, stress response of the target tissue to implanted cells, or a combination of those.

Since 2001, our group focuses on myocardial transplantation of hematopoietic stem cells that are injected into the infarct border zone of patients with previous myocardial infarction who have to undergo coronary artery bypass surgery. So far, we have treated 33 patients and observed a significant improvement of regional myocardial blood flow as well as increased global left ventricular contractility, without procedure-related complications. Based on our successful phase-I dose-escalation safety trial, we have initiated a controlled phase-II trial that will facilitate assessment of the clinical efficacy of myocardial stem cell therapy.

Notes:

S18

S18 Molecular genetics of sudden death

G.A.Danieli, Padua-I

The current knowledge on biochemical basis of sudden death is reviewed with particular reference to genes involved in cardiomyopathies and arrhythmogenic diseases. In particular results of recent advances in molecular genetics of arrhythmogenic right ventricular cardiomyopathy will be reported.

Arrhythmogenic right ventricular cardiomyopathy is emerging as a relatively common cause of sudden death in the young. Linkage analysis in families showing dominant inheritance of arrhythmogenic right ventricular cardiomyopathy succeeded in identifying eight different ARVD loci. Among them, two disease-genes have been identified so far.

Mutations in cardiac Ryanodine receptor gene (RyR2) were shown to cause ARVD2, whereas mutations in Desmoplakin gene (DSP) cause ARVD8.

An homozygous two-nucleotide deletion in Plakoglobin gene was detected in an autosomal recessive form of arrhythmogenic right ventricular cardiomyopathy associated with palmoplantar keratoderma and peculiar woolly hairs (so called Naxos syndrome).

More recently, our group identified the gene involved in ARVD1; we detected nucleotide substitutions in regulatory regions of transforming growth factor beta 3 (TGF,3) gene.

Identification of novel arrhythmogenic right ventricular cardiomyopathy genes will increase the power of the genetic screening for early diagnosis of asymptomatic carriers among relatives of affected patients.

Notes:

O01

O01 Vascular endothelial growth factor gene transfer to mice hindlimb skeletal muscle.

I.Kholova, S.Koota, P.Leppanen, J.Narvainen, S.Yla-Herttuala; Kuopio-FIN

Gene transfer of vascular growth factors is used for therapeutic formation of new vessels. Therapeutic vascular growth as such includes stimulation of angiogenesis, arteriogenesis, and lymphangiogenesis.
Materials and Methods: ApoB LDL receptor knock-out mice hindlimb skeletal muscles were injected with adenoviral gene transfer of VEGF-A (2 x 10ex12 VP/ml; n=48) and VEGF-D (2 x 10ex12 VP/ml; n=48); control hindlimbs were injected with adenoviral LacZ and saline. T2 weighted MRI was performed to follow-up edema. Animals were grouped and sacrified at days 7, 14, 28, and 42. Tranfected muscles were examined by immunohistochemistry, enzyme histochemistry, semi-thin sections, and electron microscopy.
Results and Conclusions: Both VEGF-A and VEGF-D induced neoformation of vessels, which feature luminal enlargement and branching. Angiogenesis was accompanied by tissue edema. Formation of mother vessels and glomeruloid bodies was seen in semi-thin sections. Ultrastructure showed irregularities of basement membrane indicating impaired functionality.

Notes:

O02

O02 3-D reconstruction of fetal heart: a novel approach to fetal cardiopathology.

G.Bussolati, C.Marchiò, M.Volante, A.Grua, G.Botta; Turin- I

Progress in pre-natal diagnosis of heart malformations by echocardiography are leading to challenging diagnostic problems, since pathologists have to afford the fine examination of minute cardiovascular apparatuses. In such conditions, to confirm, disprove or complement the echocardiographic pre-natal diagnosis is hard or impossible, since the size of the specimens prevents a macroscopic examination. As an alternative, we have employed paraffin embedded serial sectioning and 3-D reconstruction of fetal hearts. This process could easily and routinely be accomplished by first applying internal reference markers (tissue arrays) on the embedded heart. Histologic sections (1 every 100 microns) were collected, stained and photographed. Computer-assisted reconstruction of aligned images was accomplished. 3-D reconstructed structures could be rotated and cross sectioned so that the type of malformation could be demonstrated. Additional employment of fluorescent inks to label the atrio-ventricular and vascular cavities was also proved to be useful. In our experience, this process is relatively easy and fast, allows a comparison with pre-natal echocardiographic data, and opens new prospects to reach reliable diagnoses in fetal cardio-vascular pathology.

Notes:

O03

O03 B-catenin pathway and microsatelite instability status in sarcomas of the pulmonary artery.

A.Gaumann, B.Bode-Lesniewska, D.Zimmermann, F.Hofstadter, W.Dietmaier; Regensburg-D, Zurich-CH

Aims: The Wnt signaling pathway plays an important role in cell fate determination mediated by stabilization of the ß-catenin complex through APC. Thus, ß-catenin activation is an important step in the tumorigenesis through induction of transcription and proliferation via c-myc and cyclin D1. Since activation mutation of ß-catenin/APC has been shown to occur in a variety of tumors we investigated the expression and mutation of the involved molecules.
Methods: Expression of ß-catenin, hMLH, hMSH2, hMSH6 was examined by immunohistochemistry in 16 SPA and microsatelite instability (MSI) using the recommended reference panel for colorectal cancer. In addition, sequencing of exon 3 of the ß-catenin gene was performed.
Results: In 8 cases a membrane staining and in 3 cases additional cytoplasmic staining of ß-catenin was observed. 1 case showed some cells with nuclear staining and 3 cases were negative. Mutation analysis of ß-catenin revealed wildtype sequence of Exon 3 in all examined cases. MSI could only be detected in 1 case of the SPA. Interestingly, this case also showed nuclear staining for ß-catenin. In addition, 4 cases revealed a LOH at the APC gene locus. Nuclear expression of hMLH1, hMSH2 and hMSH6 was detected 15 cases.
Discussion: LOH of APC was the prominent observation in our series supporting the view that misfunction of this tumor supressor gene may play a role in the tumorigenesis of SPA. However, ß-catenin showed only nuclear translocation in 1 case, which was the only patient who had also MSI. Thus, alteration of the ß-catenin pathway and MSI seem to play a minor role in the proliferative activity of SPA in our series.

Notes:

O04

O04 Comparison of structure and calcification potential of kangaroo vs porcine aortic valves after glutaraldehyde fixation.

R.G.Forsyth, K.Narine, A.Waeytens, E.Claeys, C.Chery, E.Goethgebeur, M.Praet, G.Van Nooten; Gent-B

Introduction: The durability of contemporary bioprosthetic valves are limited by their propensity to calcify. Most biological valve prostheses are made from bovine or porcine tissue after glutaraldehyde fixation. Kangaroo aortic valves have been reported to calcify less than porcine aortic valves in the sheep circulatory model.
Aims: This study aimed to highlight histological and ultrastructural differences between kangaroo and porcine valves and to evaluate and compare calcification potential after fixation in 0,6%(low) or 2,0%(high) concentrations of glutaraldehyde in the rat subcutaneous model.
Materials and Methods: Ten *"de novo"* aortic valves, fixed in 2,0 % glutaraldehyde were examined (5 Kangaroo and 5 porcine valves) by light microscopy (HE, Alcian Blue, trichrome and Von Giesson´s elastin stain), transmission electron microscopy and polarized light microscopy. In the meantime two groups of Sprague Dawley rats (11 rats / group) were implanted with aortic valve leaflets after fixation in 0,6% (11 Kangaroo and 11 porcine leaflets) or 2% (11 Kangaroo and 11 porcine leaflets) glutaraldehyde. Collagen solubility was determined as a measure of the extent of fixation. From each group, animals were sacrificed after 24h and weekly for up to 10 weeks after implantation. Calcium was determined by Inductively Coupled Plasma-Mass Spectrophotometry (ICP-MSP). The localization of calcium deposits was assessed by light microscopy (Von Kossa stain). Quantitative data were analyzed using linear regression and backward stepwise analysis of variance (ANOVA) to determine predictors for calcification in the experimental model.
Results: structural comparison showed three main layers in both types of valves. The proportional thickness of each layer was different in Kangaroo (K) and Porcine (P) valves. Collagen fibers were similarly oriented with groups of parallel bundles at an angle of less than 25° to each other. In Kangaroo valves these were more compact. Proteoglycans are more uniformly distributed in Kangaroo. After 7 days of fixation, porcine leaflets fixed in 2% glutaraldehyde showed >99% and those in 0,625% glutaraldehyde >98% crosslinking. Calcification increased with time in both species. There was no significant difference in calcification between porcine and kangaroo leaflets treated with 0,625% (range: porcine; 1,7 mg Ca/mg and 186 mg Ca/mg tissue dry weight) or 2% (range 0,6 mg Ca/mg and 232 mg Ca/mg tissue dry weight) glutaraldehyde over time in either group ($p>0,05$). Furthermore there was no significant difference between groups. Calcification was observed in the spongiosa and fibrosa layers. A striking finding was the large variation in outcomes within and between animals.
Discussion and conclusion: The ultrastructure and arrangement of the structural layers of the kangaroo and porcine aortic valves indicate similar micromechanics. Kangaroo and porcine valves differ however in the relative proportions of their structural layers.

At the other hand calcification potential after fixation in high en low concentrations of glutaraldehyde does not show significant differences. Also the rat subcutaneous model showed large variations within and between animal outcomes. Although kangaroo valves are structurally more similar to human aortic valves than procine, the rat subcutaneous model does not necessarily predict prosthetic valve calcification in the circulatory system *in vivo.*

Notes:

O05

O05 Histologic determinants of diastolic dysfunction in patients with Fabry cardiomyopathy.

C.Chimenti, M.Pieroni, A.Santagostino, M.A.Russo, A.Maseri, A.Frustaci; Milan-I, Rome-I

Background: Diastolic dysfunction is the major hemodynamic abnormality of Fabry cardiomyopathy occurring, as showed by Tissue Doppler (TD) analysis, early and progressively in the disease course. Its structural basis is unknown. Methods: Eighteen pts (11 M, 7 F, 41±12 ys) affected by Fabry disease were submitted to non invasive and invasive cardiac studies including left ventricular endomyocardial biopsy. Twelve of them (7M, 5F, 45±6 ys) had moderate-severe left ventricular hypertrophy (LVH) (Group A) while 6 of them (4M, 2F, 29±7 ys) had ventricular arrhythmias and no evidence of LVH (Group B). TD velocities (Sa, Ea, Aa, and Ea/Aa ratio) were recorded at both corner of mitral annulus and compared with morphometric measurement of myocyte cross sectional area, endocardial thickness, volume fraction of myocytes and tissue fibrosis. Results: Myocyte area, endocardial thickness and fibrosis were significantly increased in Group A compared with Group B and with normal controls (myocyte area= 802±221 μm^2 in Group A, 398±75 μm^2 in Group B, 252±28 μm^2 in controls, endocardium=31±15 µm in A, 11±2 µm in B, 9±2 µm in controls, fibrosis=7±2%in A, 3.7 ±1% in B, 3,3±1% in controls). Intramyocyte glicolipids vacuoles occupied 47% of the total cell area in Group A and 20% in Group B ($p<0.001$). Myocyte area was significantly increased in Group B compared with normals ($p<0.001$), while fibrous tissue and endocardial thickness did not differ. TD abnormalities showed a positive linear correlation with myocyte area ($R=0.90$ $p<0.001$ in Group A, $R=0.86$ $p<0.001$ in Group B) and glycolipids vacuoles ($R=0.71$ $p<0.001$ in Group A, $R=0.8876$ $p<0.001$ in Group B). No significant correlation was found between TDI abnormalities and fibrosis and between TDI abnormalities and endocardial thickness in both groups. Conclusions: Myocyte hypertrophy and extent of glycolipids accumulation seem to be the major histologic determinants of diastolic dysfunction in Fabry cardiomyopathy.

Notes:

O06

O06 Fat in the right ventricle of the normal heart.

D.Tanscy, Z.Aly, M.N.Sheppard; London-UK, Harefield-UK

Fat is normally present in the human right ventricle. This fat may be confused with arrhythmogenic right ventricular dysplasia. The amount of fat in the right ventricle of 103 hearts from patients who died of non-cardiac causes was studied. 60 males and 43 females, with an age range of 6 months to 61 years. A transverse slice was taken from the right ventricle of each heart.
Results: muscle thickness of the right ventricle wall ranged from 2 to 7 mm with an average of 5 mm in males and 4.5 mm in females. In males there was an average of 2 mm of epicardial fat in the anterior wall, 4.5 in the lateral wall and 0.5 mm in the posterior wall. The fat in females were 2.5 mm, 6 mm and 0.5 mm. The boundary between the epicardial fat and muscle was well defined in 69 cases and ill defined in 25. females had more epicardial fat than males and this increased with age. Intramyocardial fat was seen in all cases, and increased in females and with age. In some cases the intramyocardial fat was confined to the outer wall and in other cases there was full thickness involvement with fat extending to the endocardial surface. Significant fatty infiltration is commonplace in the right ventricle, particularly in older female patients. The diagnosis of arrhythmogenic right ventricular dysplasia requires not only extensive replacement of the right ventricle by fat, but also fibrosis with or without inflammation.

Notes:

O07

O07 An unusual aortic valve.

L.Ffolkes, M.Hayward, D.Brull, S.Krywanych, S.Hughes; London-UK

A 48 year old Palestinian gentleman was admitted with a two month history of gradually increasing shortness of breath on exertion and a three week history of chest pain. He had a 9 year history of type 2 diabetes and complained of widespread joint pain. On this admission he was diagnosed with severe congestive cardiac failure.
An echocardiogram revealed a severely impaired left ventricle with an ejection fraction of 25%, and a calcified aortic valve with severe stenosis. An echocardiogram showed left ventricular hypertrophy but no acute ischaemic changes.
Coronary angiogram showed significant coronary artery disease. He underwent an aortic valve replacement and coronary artery bypass grafting. At operation it was noted that the entire inside wall of the aorta was covered in dark black patches which extended down into the endocardium of the left ventricle and covered the aortic valve.
Macroscopic examination revealed a calcified valve leaflet covered in black patches. Microscopic examination revealed the deposition of a brown pigment within the body of the valve, which was associated with nodules of calcium. A diagnosis of ochronosis (alkaptonuria) was suspected. This was confirmed on mass spectrometry urine analysis, which showed markedly raised levels of homogentisic acid.
Alkaptonuria is a rare hereditary disorder caused by a deficiency of the enzyme homogentisic acid oxidase. It is usually diagnosed from the triad of degenerative arthritis, ochronotic tissue pigmentation and urine that turns dark brown or black on alkalinisation. Cardiovascular disease is rare.

Notes:

O08

O08 Pelvic "tumor" growing up into right cardiac chambers.

R.Gouveia, M.Abecassis, A.Pina, R.Ribeiras, A.P.Martins; Lisboa-P

A 44 years-old female seeked medical treatment due to edema of the upper half of the body in the morning, which changed to edema of its lower half during the day. The diagnostic hypothesis was "giant myxoma" of the right atrium. The ultrasonography revealed a mass which seemed to have origin at the right adnexial area, run through the inferior caval vein and entered the right atrium, eventually merging into the right ventricle during cardiac motion. The mass was surgically removed together with the uterus, both adnexae and right ovarian vein. Grossly, it rises from the myometrium, extends to the right parametrial margin and hilar veins, and continues as a long tag. It is firm, white and fasciculated, with some hemorrhagic and cystic areas. After histological and immunohistochemical study, the final diagnosis was *uterine intravenous leiomyomatosis with extension to the right cardiac chambers*.

Notes:

O09

O09 Arterial changes in gravidic "splenic emergency syndrome".

A.Marzullo, G.Caruso, G.DiVella, A.Arpaio, M.Colonna; Bari-I

Gravidic splenic emergency syndrome is an exceedingly rare condition. It occurs due to the spontaneous splenic or splenic vessel (artery or vein) rupture. Patients typically present with sudden onset severe abdominal pain radiating to the epigastrium or left hypochondrium. The high mortality of this disease is due to massive hemoperitoneum followed by rapid hemorrhagic shock and death. We report two recent cases of pregnant women who died intraoperatively in a similar manner. Autopsies revealed in the first case (28 year old in the 33rd week of gestation) spontaneous splenic rupture; in the second (26 year old in the 40th week of gestation) rupture of a splenic artery aneurysm. Histologically, in both cases the wall of the splenic artery or of its main branches showed structural changes consisting of delamination and duplication of the lamina elastica, myointimal thickening, disarray and fibrosis of tunica media and adventitia. Factors implicated in the etiology of splenic emergency syndrome include pregnancy-related factors (hypervolemia, splenomegaly, relative reduction of the peritoneal space, hormonal changes, gravidic muscular contractions) and preexisting systemic or vascular pathology (congenital anomalies, inherited vascular disease, arterial degeneration, inflammation). In pregnancy, the synergistic action of hemodynamic and endocrine factors may induce structural changes of the arterial wall with the consequent rupture of a newly formed or pre-existing aneurysm. In these cases, the study of the splenic and splanchnic vasculature should be complete and comprehensive, to detect the precise site of hemorrhage and structural vascular changes.

Notes:

O10

O10 Sudden death in a teenager.

D.Phillips; Ashford-UK

A previously fit and healthy 13 year old female collapsed at an afternoon party and did not recover consciousness.. The event was fully supervised and there was no suspicion of alcohol or drug abuse.

At post mortem examination there were no abnormalities outside the cardiovascular system. The heart weighed 280g (approximate normal weight 180g). There was left ventricular hypertrophy and dilatation. Both cusps of the mitral valve were thickened and had a glistening yellow white appearance. One cusp of the aortic valve had a similar but less advanced pattern of thickening. Histology demonstrated expansion of loose connective tissue in the centre of the cusp and intimal thickening on the atrial aspect of the cusp. No significant changes were present macroscopically or microscopically in the ventricular myocardium. A diagnosis of mucoid degeneration with associated left ventricular hypertrophy and dilatation was made.

This is a common change in elderly adults but is seen occasionally in younger patients. In a group of 163 sudden deaths in patients less than 35 years of age it was present in 17 (10%) of cases. As in this case the majority were females. The youngest sudden death in this condition was a boy of 8 years. Circumstantial evidence suggests that it is true cause of death and some patients have myocardial abnormalities.

Notes:

O11

O11 Claudication in a 44 year old male.

H.Abdelsalam; Stafford-UK

A 44 year old male presented with a short history of unilateral lower limb claudication. The patient was otherwise fit and well and there were no risk factors for atherosclerosis. A localised popliteal artery narrowing was demonstrated on angiography. At operation a tense cystic lesion was detected and a vein interposition graft was inserted. Post operative recovery was uneventful.

The lesion was a tense adventitial cyst containing gelatinous fluid. It was physically compressing the lumen of the popliteal artery. It was lined by fibrous tissue and had a thin lining of elongated cells. These stained negatively with antibodies to endothelium but positively with HMB1E. A diagnosis of adventitial cystic disease was made.

Other uncommon causes of peripheral vascular disease include fibromuscular dysplasia, Buerger's and Takayasu's disease. Adventitial cystic disease has distinctive macroscopic and microscopic appearances. Our immunohistochemical findings support the view that it may develop from adjacent bursae or other synovial lined structures. Most, but not all cases, occur in the popliteal area.

Notes:

O12

O12 Urgent heart transplantation in a 18 year old male.

L.P.Riber-Hansen, U.Baandrup; Aarhus-DK

18 yrs old male – healthy.
One Saturday night he went out partying. Had some chest discomfort the next morning, took a pill and was relieved. In the evening the discomfort and chest pain returned. A doctor was contacted and the patient immediately admitted.
ECG showed massive anterior infarction, BP 74/56. Became haemodynamically unstable and was transferred to our hospital. Unconscious at arrival, low pressured. KAG: occlusion of LAD, its diagonals and septal branches. Thromborectomia by rescue suction, stenting and ballooning was carried out.A CPS system (Biomedicus pump) was installed.
The patient was put on the urgency-transplant-list and four days later a successful heart transplantation was done.
What had happened ?

Notes:

O13

O13 Juvenile sudden cardiac death: an autoptic analysis.

G.D'Amati, C.R.T.Di Gioia, C.Autore, M.D.Romeo, A.Lopez, C.Ciallella, P.Gallo; Roma- I

Aim. Aim of this study was to assess the causes of juvenile cardiac sudden death in the general population of the Lazio region, in central Italy.
Methods. From January 2001 to June 2004, 112 cases of juvenile sudden death (SD) (age ≥ 1 year ≤ 40 years) were consecutively referred to our Department from the Forensic Institutes and the Hospitals of our region. A complete autopsy was performed in all cases, and the circumstances of death were recorded. The results of toxicological tests were available in 40 cases. According to our study protocol, we required to examine the whole hearts when non-cardiac causes of death were excluded at autopsy. Hearts were carefully inspected and multiple samples from both ventricles, the coronary tree and cardiac valves were processed for histological examination.
Results. Of 112 cases of juvenile SD, 19 (17%) were natural deaths due to non-cardiac causes. Of the remaining 93 cases, 68 (63%) were male and 25 (37%) female subjects. The mean age was 29.7 years. Death occurred at rest in 71 cases (73%), under physical or emotional stress in 18 (19%) and was unwitnessed in 4 (8%). The whole hearts of 82 subjects (88%) were examined by our group. In 11 cases, the diagnosis was referred. Ischemic heart disease (IHD) due to coronary atherosclerosis (CAD) accounted for 14 (15%) deaths; arrhythmogenic right ventricular cardiomiopathy (ARVC) was diagnosed in 12 cases (13%), congenital heart disease (CHD) in 9 (9.6%), dilated cardiomyopathy (DCM) in 5 (5%), hypertrophic cardiomyopathy (HCM) in 3 (3.2%), hemopericardium due to aortic dissection in 3 (3.2%), mitral valve prolapse in 3, acute myocarditis in one (1%). In 3 cases the only cardiac finding was non specific left ventricular hypertrophy. Finally, in 32 cases (34%) the heart was normal or showed only mild fatty infiltration of the right ventricular anterior wall; toxicological tests were negative and death was attributed to an arrhythmic event. When available, clinical records of subjects with cardiomyopathies (n = 20) or sudden arrhythmic death syndrome (n = 32) were reviewed and first-degree relatives underwent cardiological assessment. Six of 22 families were diagnosed with inherited cardiac disease.
Conclusions. A significant proportion of juvenile cardiac SD is due both to familial cardiomyopathies and inherited arrhythmogenic syndromes without an anatomical substrate. Sudden death is often the first symptom of the underlying disease in apparently healthy subjects. Thus, a careful autopsy becomes the only diagnostic tool in these cases, providing important information to guide clinical and genetic assessment of the families.

Notes:

O14

O14 Clinical-pathological assessment of transplanted human hearts preserved by leukocyte-depleted reperfusin.

L.Dvorak, E.Honsova, J.Pirk; Prague-CZ

Early and late mortality after heart transplantation are most likely associated with leukocyte-mediated reperfusion injury to cardiac allograft endothelium in perioperative period. An introduction of leukocyte-depleting filters into the cardiopulmonary bypass circuit and the secondary blood cardioplegia circuit during heart transplantation seems to ameliorate the reperfusion damage to postischemic heart muscle. To determine the efficacy and safety of leukocyte-depleted reperfusion, 40 patients undergoing orthotopic cardiac transplantation were enrolled in a prospective, randomized clinical trial to be treated with either leukocyte-depleted reperfusion (group A; n = 20) or whole blood reperfusion (group B; n = 20). To examine whether leukocyte depletion can prevent postreperfusion ultrastructural injury, 2 perioperative myocardial biopsies were taken. In a follow-up of 12 months regular endomyocardial biopsies were taken to assess rejection episodes and simultaneously C4d complement fragment deposits associated with humoral rejection. So far obtained data suggest possitive effect of leukocyte-depleted reperfusion of human transplanted hearts, which may prevent significant reperfusion injury and improve posttransplantation graft function.

This study is realised within the grant project No. 036 of the Internal Grant Agency of the Ministry of Health, the Czech republic.

Notes:

O15

O15 Overexpression of the glucose regulated protein GRP94 enhances survival of myogenic H9c2 cells transferred into the infracted myocardium.

L.Gorza, M.Vittadello, M.Crocco, S.Gomirato, F.Zingrino, S.Sponga, G.Gerosa; Padua-I

Poor survival of grafted cells is believed to represent a major factor hindering the therapeutic effect of cell transplantation. We showed that GRP94, a stress- and calcium-binding protein localized in cardiac sarcoplasmic reticulum, is involved in protection of myocytes against necrosis due to calcium overload and simulated ischemia (Vitadello et al. FASEB J 17: 923-925, 2003). Here we demonstrate that selective overexpression of the same protein, obtained by gene transfer in rat cardiac H9c2 cells, increases resistance to apoptosis. Caspase 3 activation is about 50% lower in GRP94 overexpressing cells than in control cells, after exposure to simulated ischemia in vitro. We investigated whether a comparable protection could be observed after in vivo transfer of control and GRP94 overexpressing cells into the rat infarcted myocardium. After labelling with BrdU, about 2.25×10^6 cells, either overexpressing or not GRP94, were injected 25 min after ligation of the left coronary artery into the ischemic ventricle. By means of immunocytochemical analysis performed 24 h after, an higher number of BrdU labelled cells was detectable in the infarcted ventricles injected with GRP94 overexpressing cells with respect to ventricles injected with control cells. Furthermore, the percentage of apoptotic cells in the injected region evaluated with TUNEL appeared significantly reduced among cells overexpressing GRP94 with respect to control cells (mean and SE value $8.65\% \pm 1.57$ and $15.35\% \pm 1.08$, respectively; $p<0.01$).

These data indicate that GRP94 overexpression increases resistance against apoptosis induced by ischemia and improves survival of grafted cells.

Notes:

O16

O16 Human CD133 positive stem cells from bone marrow: a good source for therapeutic application.

P.DeCoppi, M.V.Gazzola, R.Destro, A.Angelini, M.Piccoli, F.Castello, E.Slanzi, G.Feltrin, P.G.Gamba, G.Gerosa, G.F.Zanon, C.Messina, L.Zanesco; Padua-I

Many adult tissues contain populations of stem cells that have capacity for renewal after trauma, disease, or aging. Bone marrow is the major source of adult haematopoietic stem cells. However, the adult bone marrow also contains mesenchymal stem cells, which contribute to the regeneration of mesenchymal tissues such as bone, cartilage, muscle, adipose and stroma. Antibodies against different membrane antigens have been proposed, for isolation of a defined stem cell population for therapeutic use. It is already known that the antigen CD133 defines a population of primitive and immature cells, that show haematopoietic and endothelial capacity. The aim of our study is to further evaluate the plasticity of CD133+ human progenitor cells. Isolation of CD133+ cells from either bone marrow or cord blood was performed by immunoselection method using the anti CD133+ magnetic beads. CD133+ enriched cells were plated and expanded on petri dishes and grown in presence of endothelial (EBM2 medium, VEGF), adipogenic (dexametasone, 3-isobutyl-1-methylxanthine, insulin, indomethacin) myogenic (horse serum, chick embryo extract, 5-azacytidine) and osteogenic (FBS, dexamethasone, beta-glycerophospate, ascorbic acid-2-phosphate) differentiating media. The differentiation of progenitors cells has been confirmed by studies of specific gene expression like cbfa1 (core binding factor A1) for the osteogenic induction, pparg2(peroxisome proliferation-activated receptor g2) for the adipogenic induction, MyoD and desmin expression for myogenic induction and angiopoietin for the endothelial induction.
CD133+ stem cells isolated and expanded in clinical grade conditions were mantaining stem cell potentiality. In osteogenic condition CD133+ cells were able to produce alkaline phosphatase and calcium deposits. While under adipogenic conditions, vacuoles of lipid were consistently observed, in presence of myogenic factors, CD133+ expressed MyoD and desmin. CD133+ cells cultured on matrigel and stimulated with either VEGF or other specific endothelial factors, they expressed endothelial markers and form capillary structures. Preliminary results suggest that, since CD133+ have the potential to differentiate in several cell types, they could be a good source for stem cell therapy.

Notes:

P01

P01 Macroscopical and microscopical characteristics of pulmonary veins ostia and atrial fibrillation.

I.Kholova, J.Kautzner; Kuopio-FIN

Electrophysiological studies established the critical role of pulmonary veins (PV) in the initiation of atrial fibrillation (AF). Radiofrequency PV isolation is performed also around PV ostia and a paucity of data exists about PV ostia morphology.
We studied a total of 37 autopsied hearts (24 males and 13 females aged 33-81 years) macroscopically and 9 microscopically to assess the relationship between the left atrium (LA) and PV. The history of AF was present in 17 subjects.
The LA-PV ostium was predominantly vertical with 4 separate PVs. PV diameter varied with higher values for superior PVs (36 mm in left superior PV vs. 22 mm in left inferior PV and 34 mm in right superior PV vs. 28 mm in right inferior PV). Microscopically, the thickness of myocardium at the level of ostium varied from 1 to 3 mm with high variability in completeness; continuous and circular pattern prevailed.
In conclusions, inter-individual variability exists in PV ostia in both subjects with and without AF.

Notes:

P02

P02 Infarct-related artery occlusion, tissue markers of ischemia, and increased apoptosis in the peri-infarct viable myocardium.

A.Abbate, G.G.L.Biondi Zoccai, C.Morales, R.Bussani, D.Santini, R.J.Gelpi, F.Silvestri, F.Baldi, L.M.Biasucci, A.Baldi; Naples-I, Rome-I, Buenos Aires-RA, Trieste-I

Background. Unfavorable cardiac remodeling may occur following acute myocardial infarction (AMI) in part due to cardiomyocyte loss by apoptosis associated with infarct-related artery (IRA) occlusion. It is currently unknown whether ongoing ischemia is an independent determinant for increased apoptosis in peri-infarct viable myocardium.
Methods and Findings. In order to assess the link between IRA occlusion, ischemia, and apoptosis, 50 subjects dying 4-220 days after AMI (30 with IRA occlusion and 20 with patent IRA) and 5 control subjects were selected at autopsy. Cardiomyocytes were defined as apoptotic if co-expressing TUNEL and activated caspase-3. Expression of both hypoxia-inducible factor-1 and cyclo-oxygenase-2 was assessed in the peri-infarct myocardium in 28 cases and considered as tissue marker of ischemia. Evidence of ischemia was significantly more frequent in cases with IRA occlusion (53%) than in cases with patent IRA (15%) or control hearts (0%, P=0.026). The finding of IRA occlusion and markers of ischemia identified cases with higher AR in the peri-infarct viable myocardium (12.2%[8.2-14.0], P<0.001 vs others), whereas IRA occlusion without ischemia was associated with lower AR, not significantly different from patent IRA (3.0%[1.0-7.9], vs 2.2%[1.0-5.8], respectively, P=NS). In an animal model of IRA occlusion increased AR and COX-2 expression were observed in the peri-infarct region, and a gradual decrease over time of AR in the peri-infarct region was observed.
Interpretation. Myocardial ischemia is present in over 50% of subjects dying late after AMI with IRA occlusion, and it is associated with increased apoptosis in the peri-infarct viable myocardium. Relief of ischemia after AMI may prove of benefit in preventing apoptosis and adverse cardiac remodeling.

Notes:

P03

P03 Parental cigarette smoke as a risk factor for early coronary artery disease and sudden unexpected perinatal and infant death.

L.Matturri, G.Ottaviani, R.Mingrone, M.Mauri, A.M.Lavezzi; Milan-I

Cigarette smoke is the most important risk factor for fetal and infant sudden death (SIDS). The risk of stillbirth or death during the infant's first year of life is directly related to the amount the mother smoked. There is also an association between smoke and other pregnancy problems, such as low birth weight and miscarriage. The pathogenic mechanism of smoke is referable to different factors. The combustion products of nicotine, in addition to their diffuse toxicity, are heterogeneous and cause specific lesions of the autonomic nervous system. Gaseous combustion products, such as carbon oxide, lead to atherosclerotic plaques in the cardiovascular district and in the sino-atrial and atrio-ventricular arteries. Consequently, these combustion products cause an oxygenation deficit of the common myocardium, as well as developmental abnormalities of the conducting tissue, laying the morphological substrate for arrhythmias. We recorded a high incidence of preatherosclerotic lesions in the coronaries of fetuses with smoker mothers. If the maternal smoking habit persists, juvenile plaques can be observed in the infant. These early atherosclerotic lesions can be attributed to a direct action of the combustion products of nicotine on the smooth muscle cells of the tunica media of the arterial walls and/or on the neurons, interfering with homeostasis and cell differentiation, as well as to an indirect action of hypoxemia induced by arterio- and arteriolosclerosis. Our study population included 22 stillborns and 49 infants dying suddenly and unexpectedly. All cases died *sine causa* between the 32nd week of gestation and one year of age. Samples of the myocardium and the major coronary arteries were stained with Hematoxylin-eosin and Azan. The cardiac conduction system was removed in two blocks: the first included the sino-atrial node and the *crista terminalis*, the second contained the atrio-ventricular node, His bundle down to the bifurcation and bundle branches. These two blocks were cut serially at intervals of 40-mm (levels) and stained alternately with Hematoxylin-eosin and Azan. In 55% of fetuses and in 67% of the infants, multifocal coronary early atherosclerotic lesions of varying entity were detected. The alterations ranged from focal plaques with mild myointimal thickening to juvenile soft plaques in infants reducing the arterial lumen. In 45 % of stillborns and in 75% of infants with coronary lesions the parents were smokers. A significant correlation was observed between early atherosclerotic lesions and the risk factor considered. The reduction in the coronary lumen can be such as to cause alterations in cardiac blood supply. The harmful effects of cigarette smoking are not confined to the coronaries but also affect the small and medium-caliber arteries, –including the sino-atrial and atrio-ventricular arteries. Analysis of our series suggests that parental cigarette smoking has the highest significance among the risk factors considered in the pathogenesis of sudden fetal and infant death, while the newborn's position in the crib, which has been assigned a fundamental importance in recent years, is not equally supported by anatomo-pathologic data.

P04

P04 The "Cardiovascular Registry" at the University of Padua: preliminary results from the anatomical collection of acquired heart-vessels disease.

A.Abudureheman, C.Basso, G.Thiene; Padua-I

Background. The Institute of Pathological Anatomy of the University of Padua holds one of the largest anatomical collection of cardiac specimens, coming from both autopsy and cardiac transplantation. The collection started in the 70's at the dawn of cardiac surgery and includes nearly all nosographic entities of both congenital and acquired heart disease representing nearly the whole epidemiological spectrum of modern cardiovascular pathology. Three separate collections, including more than 2000 specimens, of congenital heart disease, juvenile (<35 yrs) sudden death and cardiac transplantation have been previously classified. The aim of the present work was to reassemble also the anatomical collection of acquired heart-vessels diseases coming from routine autopsy.
Methods. A Museum for the Anatomical Collection of heart diseases has been set up and equipped with flowing cupboards with book shelves. Each specimen has been transferred in a single jar or double sack with only a small amount of formalin to avoid evaporation. Identification of each specimen is warranted by a stick on label, including registration number, date as well as Pathologic codes. A nosologic system to classify acquired heart-vessels diseases has been put forward with 12 main categories, accordingly to the main morbid entity (ie. Pericardium, Coronary artery, Myocardium, Endocardium-aorta, mitral, tricuspid, pulmonary, parietal- , Conduction system, Tumors, Vessels, Miscellanea), each subdivided in subcategories, including normal hearts. An electronic database management system has been set up for data storage and retrieval (ACCESS).
Results. A total of 687 cases, referring to the routine autopsies performed in the 7 years time interval 2002-1996, have been entered in the database and archived in the Cardiovascular Registry. Pericardial disease was present in 25%, coronary artery in 69%, myocardial in 44% (including 27% hypertensive heart disease), , valve in 30%, conduction system in 4.5%, tumors in 2% and vessels in 29%. Cardiac surgery procedures consisted of aortic valve replacement in 52 (7.5%), mitral valve in 33 (4.8%), aorto-coronary bypass grafts in 103 (15%), and aorta vascular prosthesis in 20 (2.9%). As far as interventional procedures, a pacemaker was present in 21 (3%) and coronary stent/PTCA in 44 (6.4%). Forty (5.8%) were normal hearts. As far as miscellanea is concerned, a patent foramen ovale was documented in 139 (20%), left ventricular false tendons in 165 (24%), an aneurysm of the fossa ovalis in 46 (7%) and a Chiari network in 20 (3%). A total of 130 specimens have been selected and collected separately for teaching purposes.
Conclusions. Protocols and electronic databases as well as an "ad hoc" Museum for the collection of acquired heart diseases at the University of Padua have been developed. A Cardiovascular Registry of both congenital and acquired diseases will represent the source of continuous consultation by scientists and students as part of the long-standing patavian tradition of pathologic studies in the field of cardiovascular diseases.

P05

P05 Myocardial perfusion grade and survival after percutaneous transluminal coronary angioplasty in patients with cardiogenic shock.

G.Tarantini, P.Buja, A.Ramondo, M.Napodano, C.Bilato, G.B.Isabella, R.Razzolini, S.Iliceto; Padua-I

We sought to evaluate myocardial reperfusion, and its prognostic value after percutaneous transluminal coronary angioplasty (PTCA), in patients admitted for cardiogenic shock. Lack of myocardial reperfusion despite restored coronary flow affects the survival of patients with acute myocardial infarction (AMI). Myocardial blush grade (MBG) is an angiographic measure of myocardial perfusion. We assessed MBG in 41 consecutive patients, admitted to our department within 12 hours from the onset of AMI and in cardiogenic shock.
PTCA was successful in 83% of cases, TIMI 3 was demonstrated in 22 patients (53%). MBG 2/3 was found in 14 (34%); among them 12 presented TIMI 3 flow. Compared with MBG 2/3 patients, those with MBG 0/1 were older (71 ± 11 vs 57 ± 13 years, p=0.001), had higher prevalence of diabetes (48% vs 14%, p=0.04) and hypertension (63% vs 29%, p=0.04), showed a trend toward longer ischemic time (6.1 ± 2.4 vs 4.9 ± 1.1) and had larger enzymatic infarct size (peak creatine kinase: 7690 ± 516 vs 5500 ± 2977). Mortality was higher in patients with MBG 0/1 both in hospital (81% vs 14%, p<0.001) and at follow-up (81% vs 29%, p=0.001). After adjustment by multivariate analysis, MBG 0/1 (OR 16, p=0.01) and age (OR 3.8/10 years, p=0.04) were correlated with in-hospital mortality. In cardiogenic shock after AMI, treated with PTCA, MBG 2/3 is achieved in few cases and is a strong predictor of in-hospital survival. Risk stratification after mechanical revascularization should include the assessment of restoration of myocardial reperfusion.

Notes:

P06 **Late results on survival and rehospitalization in patients undergoing different treatment for severe ischemic mitral regurgitation with multivessel coronary artery disease.**

P.Buja, G.Tarantini, F.DelBianco, M.Napodano, G.Isabella, R.Razzolini, A.Ramondo, G.Gerosa, S.Iliceto; Padua-I

Background. Management of patients with severe ischemic mitral regurgitation (MR) and multivessel coronary artery disease (CAD) is still debated. We analysed the impact of different therapeutical strategies, i.e. medical therapy (MD), coronary artery by-pass grafting (CABG) and CABG with mitral valve surgery (MVS), on outcome and the usefulness of MVS in this setting.
Methods. Between 1990 and 2002, we identified 111 consecutive patients, aged 73±8 years, with ischemic MR≥3+ (on a scale of 0 up to 4+) and multivessel CAD (≥2 major epicardial vessel) at cardiac catheterization. MR due to acute myocardial infarction (MI), mitral or aortic primary valve disease were excluded. Among 111 patients, 22 were medically treated, 50 received CABG and 39 CABG+MVS. All patients underwent a median clinical and echocardiographic follow-up of 34.9 and 14.6 months, respectively.
Results. An history of MI was present in 95% of MD patients, in 88% of CABG patients and in 85% of CABG+MVS patients and there were no significant clinical differences among groups. Left ventricular ejection fraction (MD 35±14%, CABG 38±13%, CABG+MVS 50±14%, p<0.001) and left ventricular end-diastolic volume index (MD 153±54 ml/m2, CABG 125±35 ml/m2, CABG+MVS 129±38 ml/m2, p=0.022) represented the main strumental differences among patients. Single mammary artery was used in 60% of CABG patients and in 74% of CABG+MVS patients (p<0.001). Surgical groups showed an higher in-hospital mortality (MD 13.6%, CABG 18%, CABG+MVS 17.9 %). All MD patients died within 60 months. At follow-up, CABG+MVS showed a trend to lower cardiac death (at 7 years CABG 57% vs CABG+MVS 29%, p=0.1) compared to CABG alone. After adjusting for baseline and operative differences, CABG+MVS (HR 0.35, CI 0.14-0.89, p=0.027) was independent predictor of cardiac death. There were no differences between CABG and CABG+MVS patients in term of combined cardiac death and rehospitalization rate at 7 years follow-up (CABG 90% vs CABG+MVS 91%, p=0.87).
Conclusions. In patients with severe ischemic MR and multivessel CAD, CABG+MVS predicted an improved survival but a similar rehospitalization rate compared to CABG alone.

Notes:

P07 **Alveolar gas exchange improvement in prevention of adrenaline-induced myocardial injury.**

V.A.Ohanyan, A.B.Semerjyan; Yerevan-AR

The aim of present study was to prevent the adrenaline-induced morphofunctional and metabolic cardiac alterations by applying mechanical lung venatilation (MLV).
Young mail rabbits weighing 1000-1500 gr. were divided into Gr. 1 – control animals (n=6), Gr. 2 – experimental animals (n=10) that were treated by adrenaline (Adr) hydrotartrate injected i.v. 0.2 mg/kg under Nembuthal anaesthesy, Gr. 3 – rabbits (n=10) exposed to MLV prior to Adr injection. ECG was registered by biopotential magnifier. Serum enzymes (aspartate transaminase – AST, lactate dehydrogenase – LDH, creatine kinase – CK-MB) of cardiac damage were detected 5h.following experiment. Paraffin microscopic sections of myocardium were stained by hematoxylin eosin. Statistical analysis was conducted by Student's t-test.
Results of studies showed that Adr injection caused significant reduction (by 87%, P<0.01) of heart rate in 1-3 min. following the treatment, also decrease of contraction amplitude (by 60.3%) with further extrasystoles, development of ventricular fibrillation and cardiac arrest in 5-7 min. after injection. MLV-exposed rabbits survived exhibiting only transient suppression of heart contractility. Activities of LDH, AST and CK-MB raised significantly following Adr injection (by 190%, 98% and 63% respectively, P<0.001), while after prior MLV Adr induced increase of enzyme activities only by 39%, 44.5% and 46.6% respectively (P<0.01). Microscopic examination of myocardial sections of Gr. 2 animals showed cardiomyocyte degeneration zones of necrosis, absence of linear orientation of myofibrilles that was not observed after MLV exposition.
Obtained data allow assuming that pulmonary ventilation and alveolar respiration disorders may play an important role in acute adrenaline-induced cardiac injury, and new strategies for its correction may prevent or reduce myocardial necrosis severity.

Notes:

P08 Myocardial production and secretion of chromogranin A in hypertrophic cardiomyopathy.

M.Pieroni, C.Chimenti, A.Santagostino, A.Maseri, A.Corti, A.Frustaci; Milan-I, Rome-I

Background: Chromogranin-A (CgA) is a 49 kDa acid protein present in secretory granules of neuroendocrine cells, which levels are increased in patients (pts) with chronic heart failure. We assessed the CgA serum levels and the possible expression of CgA in left ventricular (LV) myocytes of pts with hypertrophic cardiomyopathy (HCM).Methods: Twenty-one consecutive pts with HCM (14M/7F, mean age 45.1±14.4 ys) underwent cardiac catheterization with LV endomyocardial biopsy. Myocardial samples were processed for histology and immunohistochemistry with anti-CgA antibodies. Myocardial specimens from 5 HCM pts undergoing surgical septal reduction were used for total proteins extraction and ELISA studies. In all pts serum CgA and plasma brain natriuretic peptide (BNP) levels were measured and twenty one age-and sex-matched healthy subjects were used as controls. Autoptic ventricular myocardial samples were used as controls for immunohistochemistry and ELISA. Results: All pts showed normal coronary arteries, preserved contractile function and increased LV end-diastolic pressure (21.0±7.6 mm Hg). Histology confirmed the diagnosis of HCM in all cases. All pts presented an increase of both CgA (229.4±137.1 ng/ml) and BNP (150.7±96.4 pg/ml) compared with controls ($p<0.001$) and a positive correlation between CgA and BNP levels (R=0.81), CgA and LVEDP (R=0.93) and BNP and LV end-diastolic pressure (R=0.81) ($p<0.001$). Immunohistochemistry showed positive staining for CgA with granular appearance in all HCM pts but in none of controls. ELISA showed a signicant amount of CgA in the myocardium of HCM pts but not in normal myocardium. Conclusion: CgA is produced and secreted by LV myocytes in pts with HCM. CgA serum levels correlate with plasma BNP levels and LV end-diastolic pressure suggesting a stretch-induced mechanism of release. Given the negative inotropic effect on myocardial cells CgA may represent a new cardiac hormone involved in the neurohormonal regulation of myocyte function.

Notes:

P09 Association of the T-786 C endothelial nitric oxide synthase Snp with cardiovascular mortality in high risk men.

G.Maiolino, M.Zanchetta, D.Sticchi, M.Cesari, L.Pedon, A.C.Pessina, G.P.Rossi; Pauda-I, Cittadella Padua-I

Background. We previously showed that a common T-786C single nucleotide polymorphism (SNP) in the endothelial nitric oxide synthase (eNOS) gene promoter was associated with both a blunted forearm blood flow response to acetylcholine and with multivessel coronary artery disease. Therefore, we prospectively tested the hypothesis that this SNP was associated with cardiovascular (CV) outcome in the high risk patients of the GENICA study dataset.
Methods. In 991 consecutive men (n=739) and women (n=252), mean age 63±10 yrs, who underwent quantitative coronary angiography between 1999 and 2001, we determined the incidence of the composite endpoint of CV death and major CV events, including acute coronary syndromes, strokes, and need for coronary revascularization at follow-up (median 43 months, range 1-60). The T-786C SNP was determined by analysis of the melting curve of amplicons from allele specific FRET probes.
Results. We observed a total of 489 CV events, of which 84 (8.5%) were CV deaths. Kaplan-Meier analysis showed a significant effect of the eNOS SNP on the composite endpoint CV event in men ($p=0.005$) but not in women.
Conclusions. These results indicate that the T-786C SNP in the promoter of eNOS bear prognostic information in Caucasian high risk patient men undergoing coronary angiography. However, investigation of a larger cohort of female patients is necessary to conclusively rule out such an effect in women.

Notes:

P10 Histological vascular patterns of lower limb amputations in hemodialysis patients.

R.Gouveia, R.Birne, T.Adragao, A.Pina, J.Nogueira, M.J. M.J.Pais, H.Messia, A.P.Martins; Lisboa-P

Lower limb amputations are more frequent in hemodialysis (HD) patients (pts) than in general population. The aim of our study was to evaluate histological characteristics of vascular disease in lower limb amputations performed in HD patients. Eleven consecutive patients (8 M and 3 F) with mean age of 59±13 years, mean low-flux hemodialysis duration of 61.6±53 months and with gangrene lesions were submitted to lower limb amputations at different levels. Diabetes mellitus was present in 7 pts (64%). Partial or totally occlusive lesions consisted of fresh and/or organized luminal thrombi in 10 pts (91%) and cholesterol emboli in 1 patient. Other vascular lesions documented both in macroscopically damaged and undamaged areas were fibrointimal hyperplasia in 6 pts (55%), type II/III atherosclerotic plaques (American Heart Association classification) in 4 pts (37%), reduplication of the internal elastic laminae in 3 pts (27%). Calcifications at the wall of small and medium sized arteries were present in 7 pts (64%). These calcifications were irregular and interested the media in 7 pts and also the internal elastic laminae in 5 of the 7 pts. Atherosclerotic plaques were present in 3 of the 7 pts with medial calcifications. Medial calcifications were associated with the presence of diabetes mellitus (p=0.003). Atherosclerotic plaques were associated with internal elastic laminae reduplication (p=0.02). In conclusion, in these patients (HD), occlusive arterial disease was associated with different vascular patterns. Medial calcification was the most frequent finding and was associated with atherosclerosis only in 43% of cases.

Notes:

P11 Lipid rich atheromatous core with thin fibrous cap as a determinant for neointimal formation among in-stent restenosis.

H.Ishibashi-Ueda, K.Ohta, H.Hao, Y.Ikeda, M.Yamagishi, C.Yutani; Osaka-J

The relationship between burden of native atheromatous plaque, especially lipid rich core amount and neointimal hyperplasia causing in-stent restenosis would be clarified by this study.
In-stent restenosis is largely due to neointimal hyperplasia. However, causative factors of neointimal growth are not fully clarified. We investigated stented coronary arteries histopathologically to evaluate the relation between the amount of native atheromatous plaque and plaque characters to neointimal hyperplasia. Thirty coronary artery segments with various metallic stents cut into 89 sections were obtained from 25 autopsy cases. In-stent restenosis was observed in 37 sites and the remaining 52 sites did not have restenosis. Our results showed that following stent deployment in coronary arteries, there was significant correlation between the extent of lipid rich core and the formation of neoinima ($y=0.62x+0.18$, $r=0.79$, $p<0.001$). The presence of large lipid rich core (Hazard Ratio, HR=2.48, 95% Confidence Intervals, 95%CI :1.22-5.03, p=0.011), and thin fibrous cap (HR=3.501, 95% CI: 2.015-6.101, $p<0.0001$) were independent factors of restenosis, although external elastic membrane area and plaque area were not related to the occurrence of restenosis.
Moreover, atheromatous plaques with thin fibrous caps were more likely to evoke thrombus formation, inflammatory response, and plaque rupture causing neointimal hyperplasia. In conclusion, the degree of intimal hyperplasia after stenting must strongly depend on the amount of lipid rich core of atheromatous plaque and the characteristics of coronary arteries.

Notes:

P12 Plaque haemorrhage, atheroma and C-reactive protein: an "in vivo" study in stable and unstable angina.

A.Celeste, E.Birscic, E.Tessitore, M.Crudelini, A.Alberti, A.Pucci; Turin-I

Background: Intraplaque haemorrhage is common in advanced coronary atherosclerotic lesions. Glicophorin A is a component of red cell membrane which can bind to macrophage scavenger receptor, and it has been demonstrated in fibroatheromas of coronary lesions in sudden cardiac death. Moreover, human atherosclerosis has many characteristics of an inflammatory disorder and the acute phase protein C-reactive protein (CRP) has been proposed as predictive factor of coronary events.
Methods: We investigated possible correlations between plaque morphology, Glicophorin A immunoreactivity, serum CRP levels and clinical instability in 100 patients affected by unstable (n=53) or stable (n=47) angina and undergone directional coronary atherectomy (DCA). Culprit lesions obtained by DCA were paraffin-embedded and investigated by conventional histology, morphometry, histoenzimatic (chloroacetate esterase staining, detecting mast cells and neutrophils) and immunohistochemical (for CD68, CD34, smooth-muscle cell actin, UCHL-1, L26 antigens and for Glicophorin A, respectively) techniques. The presence and extension of plaque components were evaluated and immunoreactivity was graded semiquantitatively by using a scale from 0 to 4.
Results: Plaques with more represented atheroma, inflammation (particularly, macrophages and mast cells) and angiogenesis were also more positive for Glicophorin. By statistical analysis (using t-Student and ˜2 tests) we observed statistically significant correlations between presence and extension of fibroatheroma with Glicophorin immunoreactivity, PCR levels and clinical instability. CRP showed also a significant correlation with clinical instability (p=0.001).
Conclusions: In the present study, we observed a significant correlation between plaque morphology, and particularly fibroatheroma, Glicophorin immunoreactivity, serum CRP levels and clinical instability; in particular, plaque haemorrhage was associated with UA.

Notes:

P13 "In vivo" coronary histology and lipid-lowering therapy.

L.Formato, A.Celeste, M.Crudelini, C.Moretti, P.G.Greco-Lucchina, E.Tessitore, I.Sheiban, A.Pucci, G.P.Trevi; Turin-I

Background: Lipoprotein abnormalities are a major risk factor for cardiovascular disease. However, atherogenesis involves also an inflammatory response in the arterial wall. Statin drugs have been shown to reduce not only atherogenic lipoproteins but also cardiovascular morbidity and mortality by causing a reduction in atherogenic lipoproteins and in C-Reactive Protein.
Methods: We investigated 25 specimens of directional coronary atherectomy performed in 25 patients affected by Stable Angina (SA, n=11), Unstable Angina (n=8) or recent AMI (n=6). Three patients' groups were established: patients with lipoprotein abnormalities undergoing statin therapy (n=12, Group A) or without statin therapy (n=6, Group B), and patients without lipoprotein abnormalities (n=7, Group C). Lesions were classified according to AHA criteria and percentages of fibroatheroma, fibrocellular component, plaque hemorrhage (evaluated as immunoreactivity area for Glicophorin A), thrombus and calcifications were assessed. Immunoreactivity for monocyte-macrophage CD68 and endothelial CD31 antigens were semiquantitatively scored (using a scale from 0 to 4).
Results: Fibroatheroma was present in all cases (6/6, 100%) of Group B, in 50% (6/12) of Group A and in 28% (2/7) of Group C. CD68 immunoreactivity reached higher score values in Group B, followed by Group A, then by Group C (mean score value: 2.3 – 2.0 and 0.7, respectively). The same trend was observed for CD31 positivity (mean score value 2.3 -1.4 e 0.14 in Group B, A and C, respectively). With regard to clinical diagnosis, fibroatheroma was observed in 69% (9/13) of patients with UA/AMI and in 45% (5/11) of patients with SA. Immunoreactivity for Glicophorin A, expression of plaque hemorrhage, reached higher percentage values in UA/AMI patients compared to SA.
Conclusions: In this preliminary "in vivo" study, lipoprotein abnormalities appeared related to plaque histology such as statin drugs seemed to influence the plaque composition; finally, plaque hemorrhage and fibroatheroma resulted more represented in unstable clinical conditions (UA/AMI), our findings furtherly supporting the hypothesis that accumulation of erythrocyte membranes may represent a potent atherogenic stimulus and increase the risk of plaque destabilization.

Notes:

P14

P14 Pre-clinical trial of a self-xpandable nitinol stent.

M.Prunotto, M.Galloni, S.Gaggianesi, C.Isaia, E.Pasquino; Turin-I

Pur pose: Testing the biocompatibility and effectiveness of a nitilnol self-expandable carbon-coated stent system (Carbostent Flype, Sorin Biomedica, Italy) in the porcine model at different follow-up periods.
Methods: Sixteen minipigs received in iliofemoral segment 26 Carbostent Flype (C.F.) and 6 Smart (S.) (Cordis, USA), as a control stent. Explants were performed after 7, 30, 90 and 180 days of follow-up. Comparative histological, immunohistochemical, histomorphometric and scanning electron microscopy (SEM) analyses, to assess inflammatory reaction, endothelialization process, neointimal growth and composition, were performed.
Results: All stents were successfully implanted. No mural thrombi were observed at gross inspection, by angiography or histological examinations. The neo-intima preented homogeneous growth and moderated thickness at 30 (C.F.: 0.38±0.36 mm, S.: 0.31±0.12 mm) and 90 days (C.F.: 0.33±0.30 mm, S.:0.19±0.08). At 180 day follow-up the neointimal proliferation was respectively 0.27±0.25 mm for C.F. and 0.58±0.23 mm for S.. Histological data validations of vessel endothelialization was obtained with SEM for 7-day follow-up group.
Conclusion: This study demonstrated that C.F. express good technical features at implant. The biological response highlighted good and comparable results between the two devices after 30 and 90 days, while at 180 days C.F. showed a better healing process resulting in a thinner neointimal deposition.

Notes:

P15

P15 Antibody as a possible mediator of apoptotic events in xenograft rejection.

F.Besenzon, M.Seveso, F.Calabrese, G.DeBenedictis, P.Rigotti, E.Cozzi, G.Thiene, E.Ancona; Padua-I

Acute humoral xenograft rejection (AHXR), a vexing outcome of organ xenotransplantation, has been associated with apoptosis of endothelial cells in the graft. Recent in vitro work has demonstrated the capacity of antibody to induce apoptosis. In this study, we wish to examine whether antibody may play a role in the apoptosis associated with AHXR of pig xenografts transplanted into primates.
Methods: Seven nephrectomised cynomolgus monkeys received an hDAF porcine renal xenograft and were immunosuppressed with cyclophosphamide, cyclosporine A, mycophenolate sodium and steroids. Porcine aortic endothelial cells (PAEC) from hDAF transgenic pigs were incubated for 24 and 48 hrs with different concentrations of primate sera collected pre-transplant and at the time of euthanasia. Analysis of apoptosis was undertaken by flow cytometry for the appearance of a sub-diploid DNA peak using Propidium Iodide (PI) and via Annexin-V staining to assess the exposure of phosphatidylserine on the outer leaflet of the cell membrane. In addition, the increase of caspase-3,-7 activity was determined in a fluorimetric assay. Responses to swine recombinant TNFa, camptothecin and normal human serum (NHS) were used as positive controls.
Results: With regards to the PI analysis, TNFa and camptothecin led to apoptosis in 14-32% of PAEC. NHS was able to induce apoptosis in up to 28% of PAEC. Only post-transplant serum from primate C130 was able to induce apoptosis in up to 12% of PAEC. As far as the Annexin-V analysis is concerned, post-transplant sera of 3 primates were able to induce between 5 and 10% apoptosis. Caspase analysis confirmed the increase of apoptosis in the terminal sera compared to pre-transplant sera in 2 primates. This increase was 2 and 3 fold, respectively.
Conclusion: Our data indicate that apoptotic events observed in AHXR, occurring when pig xenografts are transplanted into primates, may at least in part, be mediated by the elicited humoral immune response.

Notes:

P16 Distal protection during carotid artery stenting in symptomatic and asymptomatic patients.

F.Mistrorigo, A.Angelini, B.Reimers, M.DellaBarbera, C.Cernetti, G.Pasquetto, M.Valente, P.Pascotto, G.Thiene; Padua-I

Background:Embolization of particles generated during endovascular procedure on carotid artery plaques represents the most relevant source of post procedural stroke or death. Numerous cerebral protection devices have been proposed to limit the acute neurological complications. Aim of our study was to assess the magnitude of microembolization during carotid arteries stenting in symptomatic and asymptomatic patients and to investigate the relation between clinical and angiographic variables and pathological data.
Methods: Elective carotid stent implantation with the use of a distal filter protection was performed in 81 patients with a >70% stenotic lesions (mean 82.2 ±10,5%) of the internal carotid artery. Computed histomorphometric analysis was performed on the filter retrieved after the procedures and the following quantitative indexes of embolization burden were assessed: the % of the area of the filter membrane occupied by debries, the number of captured particles, the two longest perpendicular diameters of the largest particles. Baseline clinical and angiographic characteristics and procedural variables were assessed and correlated to the pathological parameters.
Results: Twenty-nine patients had previous, lesion related, neurological symptoms, 52 patients were asymptomatic. Mean age of the symptomatic and asymptomatic patients was 73,5±7,9 and 70±8 years, respectively (p=n.s.).
Debris were present in 90% and 88% of symptomatic and asymptomatic patients, respectively (p=n.s.). Symptomatic patients presented larger particles (maximal longitudinal diameter: 1839.5±961 µm vs 1374.3±783 µm, p= 0.04) and larger mean surface area covered with material (31.6±16,5% vs 23.7±14,5%, p= 0.04) compared to asymptomatics. Angiographically ulcerated plaques in symptomatic patients produced larger particulates when compared to those in asymptomatics (maximal longitudinal diameter: 2080±1006 µm vs 1388.2±820 µm, p= 0.03).
Conclusions: Particulate debris was collected in a high percentage of distal protection filters during carotid artery stenting . In symptomatic patients an increased amount of debris was found in the protection filter, and symptomatic plaques potentially embolize larger particles able to produce symptoms.

Notes:

P17 Contrast-enhanced transthoracic echocardiographic doppler assessment of coronary flow velocity reserve in heart transplant recipients: lack of correlation with acute rejection.

F.Tona, A.L.P.Caforio, A.Angelini, R.Montisci, C.Sarais, A.Gambino, G.Feltrin, M.Ruscazio, A.Vinci, M.G.Leone, G.Gerosa, G.Thiene, S.Iliceto; Padua-I, Cagliari-I

Histological findings suggest that the coronary microcirculation is impaired and that myocardial ischemia might be a component of acute cardiac allograft rejection (AR). Functional studies have however given controversial results. We assessed the potential role of noninvasive coronary flow reserve (CFR) evaluation as predictor of acute cardiac AR.
Methods: We studied 13 heart transplant (HT) recipients (9 male, aged 56 ± 8 years at HT) with normal coronary angiograms and without wall motion abnormalities and hypertrophy by transthoracic echocardiography (TTE). Coronary blood flow velocity in the left anterior descending coronary artery was noninvasively detected by contrast-enhanced Doppler TTE, at 7 ± 4 months after HT, within 6 hours from an endomyocardial biopsy (EMB). CFR was calculated by the ratio of hyperaemic diastolic peak velocity (DPV) during adenosine infusion to baseline DPV. A CFR >2 was regarded as normal. CFR evaluation was made blindly from EMB results. Comparison of means was made by Student's t test. A p value <0.05 was considered to be significant.
Results: Four out of 13 patients (pts) (30%) had acute AR episode ≥ 3A (ISHLT grade) (group A) while 9 pts (group B) were free from acute AR. Septal and posterior left ventricular wall thickness were similar in the two groups (10 ± 0.96 vs 10.4 ± 1.25 mm; 9.25 ± 0.5 vs 9.86 ± 0.69 mm respectively, p= NS). Blood haemoglobin, heart rate, systolic and diastolic blood pressure were also similar. CFR was normal in all pts and did not differ in rejectors vs nonrejectors (3.3 ± 0.2 vs 2.99 ± 0.4, p=NS).
Conclusions:We failed to demonstrate impaired CFR during acute AR by noninvasive contrast-enhanced Doppler TTE. The absence of CFR impairment during acute AR may be useful if this method is used to identify an abnormal intramyocardial coronary circulation in cardiac allograft vasculopathy.

Notes:

P18 The pathology of sudden cardiac death: a specialist centre referral experience.

A.Fabre, M.N.Sheppard; London-UK

Sudden death is an important cause of death in the community often due to coronary atherosclerosis. As a specialist centre, we undertook a systematic review of all cases of sudden cardiac death between January 1994 and December 2002. The cohort included 188 women [age range15-75, mean 31] and 293 men [age range 15-81, mean 32].
55% (267/481) of the cases had a normal heart and were labelled sudden adult death. This group included cases in which there was a history of asthma (n=5), diabetes mellitus (n=3), schizophrenia (n=4), anorexia (n=4), alcohol consumption and fatty liver (n=8) and epilepsy (n=8). One fifth of the cohort (21%) had diseases of the myocardium: HCM (n=25), DCM (n=8, including alcohol and post-partum DCM), interstitial fibrosis (n=29) and other cardiomyopathies (n=4), idiopathic hypertrophy of the left ventricle (n=9), ARVD (confirmed in 8, suspected in 7 as insufficient material was referred for assessment). Myocarditis was diagnosed in 20 cases (4.1%), sarcoidosis in 8 (1.6%).Anomalies of the coronary arteries (CA) included anomalous origin (n=5), bridging of the LAD (n=4), dissection (n=2), lipoma (n=1). Coronary spasm was suspected in 6 cases. A vasculitic process was diagnosed in 3 cases. Rare entities such as mesothelioma of the AV node, metastatic adenocarcinoma to the heart, ITP-related necrosis, lipid hyperplasia of the interventricular septum were also recorded.
Conclusion: The cardiac pathology of sudden death is variable, and extensive sampling is required. In more than half of our cases, the heart was normal and represents true sudden adult death, which is being recognized and accepted by both pathologists and coroners. Because of a genetic link to sudden death (long Q-T and Brugada syndromes, cardiomyopathies etc,), screening of family members is essential.

Notes:

P19 The histopathology of aortitis of the thoracic aorta and its differential diagnosis with clinico-pathologic correlation.

A.Barbour, M.N.Sheppard; London-UK, Adelaide-AUS

Thoracic aortic aneurysms can be caused by aortitis, non-inflammatory medial changes, atherosclerosis or chronic dissection. We had difficulties in reporting such specimens due to overlapping histopathological features between these entities. We subsequently reviewed the histopathology and clinical notes of 17 cases of aortitis of the thoracic aorta reported between 1991-1999, and compared the findings with 26 cases of other pathologies which could be considered in the differential diagnosis in an attempt to make clearer the diagnostic features of each. Aortitis can show a variety of medial inflammatory patterns and there is usually associated chronic wall damage. Most cases had no history of a related pre-existing disease. Changes classically described as “cystic medial necrosis” can be seen in aortitis but marked intimal fibrotic thickening and vascular extension into the inner media, as well as medial inflammation, are useful features to help differentiate these conditions. The clinical history is particularly helpful in chronic dissection as the histopathological features can mimic aortitis and atherosclerosis. Atherosclerosis may occur secondarily to other conditions but may of course occur independently. Some cases are unable to be classified.

Notes:

P20 Three-dimensional electroanatomic voltage mapping for diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: correlations with endomyocardial biopsy.

L.Leoni, D.Corrado, C.Basso, B.Tokajuk, B.Bauce, A.Ramondo, L.Daliento, A.Nava, G.Buja, S.Iliceto, G.Thiene; Padua-I

Background: 3-D electroanatomic voltage mapping offers the potential to identify low-voltage areas that correspond to regions of right ventricular (RV) myocardial loss and fibrofatty replacement in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D). Methods and Results: Thirty-one consecutive patients (22 males and 9 females, aged 30.8±7 years) who fulfilled the ESC/ISFC Task Force criteria for ARVC/D diagnosis after "non-invasive" clinical evaluation, underwent further "invasive" study including RV electroanatomic voltage mapping and endomyocardial biopsy (EMB) to validate the diagnosis. Multiple endocardial, bipolar electrograms (175±23) were sampled during sinus rhythm from RV inflow, mean ventricular body, apex, and outflow. Twenty patients (Group A, 65%) had an abnormal RV electroanatomic voltage mapping showing one or more areas (mean 2.25±0.7) with low voltage values (bipolar electrogram amplitude <0.5 mV), surrounded by a border zone (0.5-1.5 mV) which transitioned into normal myocardium (>1.5 mV). Low voltage electrograms appeared fractionated with significantly prolonged duration and delayed activation. In 11 patients (Group B, 35%) electroanatomic voltage mapping was normal, with preserved electrogram voltage (4.4±0.7 mV) and duration (37.2±0.9 ms) throughout the RV. The two subgroups did not differ with regard to age, sex, disease duration, ECG repolarization changes, ventricular arrhythmias, RV structural/functional abnormalities, left ventricular involvement, and inducibility at programmed ventricular stimulation. Low-voltage areas in patients form Group A corresponded to echocardiographic/angiographic RV wall motion abnormalities and were significantly associated with myocyte loss and fibrofatty replacement at EMB ($p<0.0001$) and familial ARVC/D ($p<0.0001$). Patients from Group B had a sporadic disease and histopatologic evidence of inflammatory cardiomyopathy ($p<0.0001$). During a mean 3.4 year follow-up, 11 patients (55%) with electroanatomic low-voltage regions received an ICD due to life-threatening ventricular arrhythmias, whereas all but one patient with normal voltage map remained stable on antiarrhythmic drug therapy ($p=0.02$). Conclusions: Electroanatomic voltage mapping enhanced accuracy for diagnosing ARVC/D: 1) by demostrating low-voltage areas which were associated with fibrofatty myocardial replacement; 2) by identifying a subset of patients who fulfilled Task Force diagnostic criteria, but showed a preserved electrogram voltage, an inflammatory cardiomyopathy mimicking ARVC/D, and a better arrhythmic outcome.

Notes:

P21 Concomitant pulmonary venous changes in females with hypertensive pulmonary arteriopathy.

O.Leone, N.Galié, A.Manes, L.Negro, G.G.Pietra; Bologna-I

The updated pathological classification proposed at the 2003 Venice Third World Symposium on Pulmonary Arterial Hypertension categories vasculopathies of pulmonary hypertension (PH) as 1) Pulmonary Arteriopathy (PA), 2) Pulmonary Occlusive Venopathy (POV) and 3) Pulmonary Microvasculopathy, focusing on the main vascular anatomical section involved by pathological changees (arterioles, capillaries or veins) and marking concurrent alterations in other areas, in accordance with the "Revisited Clinical Classification of PH". Our study aims to detect the percentage of coexisting venous changes in PA and to investigate the possible clinical significance of concurrent arteriopathy/venopathy.
Methods: The autoptic case records of 13 patients (median age 31.95±19.34), 7 females and 6 males affected by PH were reclassified using the new classification. PH was idiopathic in 10 patients and associated to risk factors in 2 cases. Vascular pathology was evaluated in multiple sections stained with HE, Mallory thricrom and elastic Weigert-Van Gieson.
Results: The 13 cases were classified as: 5 cases of PA without venous changes (group I, all males, median age 24.68±23.51, age-range 18 weeks-55 yrs); 6 cases of PA with coexisting venous narrowing or obstructive changes (group II, all females, median age of 35.83±17.17, age-range 21-55 yrs) and 2 cases of POV associated to various degree of arterial alterations (group III). The main differences between patients of groups I and II were gender, median-age and age-range. No differences between idiopathic and associated to risk factor forms or between the histological spectrum of arterial lesions were seen.
Conclusions: Our results clearly demonstrate that 2 subgroups emerged in category PA: the first typical of young and middle aged females and characterized by coexisting venous changes and the second characteristic of males with exclusively arterial lesions. The Authors discuss this different assessment of vasculopathies and the possible clinical implications.

Notes:

P22 Transmural coronary inflammation "trigger" of instable plaques rupture.

E.Maresi, R.Midulla, E.Orlando, V.Cospite, G.Fazio, R.Porcasi, C.Trapanese, F.Pellegrino, P.Procaccianti; Palermo-I

Coronary thrombosis is in most instances initiated by the rupture of an unstable atherosclerotic plaque (UAP). In UAP lymphocytic infiltrates can be observed in the fibrous cap, in the adventitia and less frequently in the tunica media. The inflammation occurs secondary to the continuous lipid deposition in the intima and/or to various infectious stimuli, which overlay the atherosclerotic process and, just as conventional factors (hemodynamic stress, etc.), may determine the rupture of the UAP. In this study, the authors provide two *post-mortem* cases of sudden cardiac death caused by rupture of an UAP, triggered by a transmural inflammatory process (coronaritis). CASE REPORT – *Case 1:* male subject, 44 years old, apparently in good health until 1 hour prior to death. At autopsy the main medical findings were cardiac in nature and consisting of acute occlusive trombosis occurring in atherosclerotic plaques localized in the left anterior descending (LAD) and in the right coronary arteries. Histologically the occluded coronary vessels showed transmural inflammatory infiltrate and rupture of UAP. *Case 2*: male subject, 38 years old, affected by symptomatic dilatative cardiomyopathy died during the lunch suddenly and unexpectedly. At autopsy the main medical findings were cardiac in nature. They consisted of myocardial lesions ascribable to dilatative cardiomyopathy and occlusive thrombosis of the LAD. Histologically the LAD showed transmural inflammatory infiltrate and rupture of UAP and anterior free wall of left ventricle revealed acute ischemic myocardial lesions. CONCLUSION – These cases report confirms the hypothesis that inflammation plays a key role in promoting the formation of an UAP as well as its rupture.

Notes:

P23 Coronary artery emboli.

S.D.Cohle; Grand Rapids-USA

Coronary artery emboli are a rare cause of sudden death. From the autopsy records of four institutions we identified nine cases of fatal coronary emboli in the epicardial branches. The sources of the emboli included three cases of nonbacterial thrombotic endocarditis (one in a patient with gastric carcinoma, one in a patient with a unicuspid aortic valve, and one in a patient with a quadricuspid aortic valve), two cases of infective endocarditis, and one case each of an atheromatous plaque of the ascending aorta, a probable left atrial appendage thrombus, a mural thrombus in a patient with a myocardial infarct, and calcifications superimposed upon an aortic valve damaged by rheumatic fever. A literature review of series of cases reported in the pre-1960 era, the 1970's and 1980's showed a decrease in emboli from infective endocarditis, and a rise in emboli originating from prosthetic valves. The etiologies of our cases suggest that infective endocarditis remains a common source of coronary emboli and that nonbacterial thrombotic endocarditis may be a more important cause of coronary emboli than suggested by prior series. Emboli arising from aortic atheromas have not been reported in recent years.

Notes:

P24

P24 Retrieval analysis of mechanical heart valve prostheses: a 30 years experience at a single institution.

T.Bottio, G.Rizzoli, G.Gerosa, G.Thiene; Padua-I

Background and Aim: Mechanical valve prostheses are known to provide a durable and effective solution to restore diseased heart valves function. Implant retrieval analysis represents one of the most crucial post-clinical control phase of such devices. This study was designed to determine the usefulness of mechanical heart valve retrieval analysis as part of testing protocols for mechanical heart valves in the clinical practice.

Material and Methods: Between 1970 and 2003, 4326 patients (pts) underwent heart valve replacement with a mechanical prosthesis at Padua University. One-hundred and fifty-nine mechanical prostheses were explanted at reoperation. Overall we collected 9 caged-ball (8 Starr-Edwards valves, 1 Smeloff-Cutter), 3 caged-disk (1 Kay-Shiley, 1 Beall-Surgitool, and 1 Hufnagel), 108 tilting disc valve prostheses (47 Sorin monocast, 33 Lillehei-Kaster, 23 Bjork, 3 Medtronic-Hall, 1 Omnicarbon and 1 Omniscience), and 40 bileaflet valves (26 St. Jude Medical, 6 Carbomedics, 4 Sorin Bicarbon, 3 Duromedics, and 1 TRI-Technologies). The devices were investigated for primary failure (structural defects, fractures, asymmetries or sites of abrasive wear onto the opening-closing system, pivot widening, disc notching and ball imbibing phenomena), and secondary failure (pannus tissue overgrowth, thrombus formation, and vegetations).

Results: Thrombosis and pannus-tissue overgrowth were the major causes of failure for first generation prostheses. Perivalvular-leak led to prosthesis replacement in 41% of tilting disk and 49% of bileaflet valves. Pannus tissue overgrowth and thrombosis were the second cause of tilting disc valve dysfunction, whereas for bileaflet valve the second cause was valve endocarditis. Mechanical failure was the cause of explant for 3 caged-prostheses due to ball imbibing and disc notching, and for 6 tilting disk valves due to disk notching (4 Bjork) and pivots widening with loose disk movements (2 Sorin monocast). No one bileaflet valve failed due to mechanical reasons except for one TRI-Technologies valve which presented a disk escape.

Conclusion: Implant retrieval analysis may play a substantial role as part of quality control of implanted prostheses. A better understanding of failure mechanism of heart valve prosthesis once implanted in vivo may lead to a complete redesign of the implants by manufacturers.

Notes:

P25

P25 Molecular diagnosis of acute myocarditis causing sudden death in young people.

E.Carturan, C.Basso, F.Calabrese, G.Thiene; Padua-I

Background. Although myocardits usually presents with signs of pump failure and ventricular dilatation as to lead to progressive systolic dysfunction, sudden death (SD) may be the unpredictable fatal clinical presentation in subjects with apparently normal hearts. Aim of our study was to assess the prevalence of viral myocarditis as a cause of SD in the young.

Methods and Results. In the time interval 1980-2004, 413 young people (<35 yrs of age, excluding SIDS) who suffered cardiac sudden death (SD) were investigated by a throughout postmortem gross and histologic protocol and 65 (16%) (39 male and 26 female, mean age 21.7±8.7 yrs) were due to acute myocarditis. Since 1998 molecular analysis on paraffin sections (26) or fresh tissue (4) of the myocardium have been also applied in a consecutive series of 30 SDs due to acute myocarditis to search for common cardiotropic DNA and RNA viruses. Sequencing analysis was used to characterize the viral genotype. A history of flu-like illness in the previous days was documented in 11 (37%). None of them had cardiac symptoms or signs either in the past or in the preceding days. At postmortem, the heart was grossly normal in all, the inflammatory infiltrate was either diffuse (11, 37%) or focal (19, 63%), and at immunohistochemistry was lymphocytic in 19 (67%) and polymorphous in 11 (33%). Clear-cut evidence of myocyte necrosis was present in 15 (50%). Nucleic acids extraction was adequate in 26 (87%) and 17 (65%) had evidence of viral infection: enterovirus in 13 (either isolated -9- or associated with cytomegalovirus in 2, and Epstein Barr virus or Epstein Barr virus and cytomegalovirus one each), parvovirus B19 in 2 (associated with herpes and Epstein Barr virus, respectively), cytomegalovirus and adenovirus one each. No difference was found in terms of myocyte necrosis and inflammatory infiltrate type and extent when comparing viral vs non viral myocarditis (all p=NS).

Conclusions. Acute myocarditis is a no so rare cause of arrhythmic SD in previously healthy young people with grossly normal heart and it is viral in origin in the majority of cases. Double/multiviral infection are common, a feature in keeping with the aggressive pattern of arrhythmogenic myocarditis. Although enterovirus are the most frequent (two-thirds of cases), other virus are detected highlighting the need for a comprehensive molecular pathology screening.

Notes:

P26

P26 Determinants of heart failure in hypertrophic cardiomyopathy.

F.Bobbo, P.Melacini, A.Angelini, C.Basso, S.Iliceto, G.Thiene; Padua-I

Purpose: Progressive heart failure (PHF) is the second cause of mortality and the main expression of morbility in hypertrophic cardiomyopathy (HCM). We sought to identify determinants of PHF in a large population of HCM patients and pathological substrates of heart failure death (HFD).
Methods: 293 HCM patients were diagnosed and followed-up for a mean of 7±6 years. End-points were PHF and HFD. Univariate and multivariate analysis were based on clinical and echocardiographic variables. Pathological evaluation was performed in 12 hearts.
Results: 50 patients (17%) developed PHF, including 18 HFD (10 deaths and 8 heart transplantations). HF mortality were 6% at 7 yrs. Left atrial dimension resulted as independent predictor for PHF, ejection fraction<50% for HFD and atrial fibrillation (AF) for both PHF and HFD. Five different forms leading to heart failure were identified: 1-"end-stage" with ejection fraction<50% in 14 patients (5%); 2-secondary to AF in 15 (5%); 3-secondary to left ventricular outflow tract obstruction in 11 (4%); 4-"restrictive" with mild hypertrophy, huge atrial enla enlargement and restrictive filling pattern in 7 (2%); 5-rare forms without obstruction and at sinus rhythm in 3 (1%). Among 12 heart macroscopically and microscopically evaluated, severe interstitial fibrosis was found in all cases. Replacement type-fibrosis was associated to "end-stage" form in all hearts and to AF form in 2/5 hearts (40%).
Conclusion: Progression to severe HF in HCM is due to a variety of pathophysiologic mechanisms: systolic dysfunction associated with marked myocardial scarring, atrial fibrillation, left ventricular outflow obstruction, and restrictive form unassociated with obstruction.

Notes:

P27

P27 Role of magnetic resonance imaging in the arrhythmic risk stratification in repaired tetralogy of Fallot.

G.Russo, A.F.Folino, L.Cacciavillani, F.Corbetti, B.Bauce, L.Daliento; Padua-I

Background: patients operated on for tetralogy of Fallot (TOF) in late '70-80 years are at risk of sudden death and major ventricular arrhythmias in late follow-up, above all due to the presence of a large right ventriculotomy and fibrous tissue. A lot of non-invasive parameters have been proposed to identify patients at high risk of major arrhythmic events. Aim of this study was to see whether cardiovascular magnetic resonance imaging (MRI) with gadolinium injection could offer further information in patients who had a clinical history of sustained ventricular tachycardia (SVT).
Methods: 24 consecutive patients (11 males, mean age 34 ± 9 yrs,) have been underwent MRI since September 2003. Among these, 8 patients had at least one episode of SVT during a mean period of 18 ± 6 yrs after repaired of TOF. They were treated with anti-arrhythmic drugs. All patients during MRI had gadolinium injection and images were acquired at first pass and after ten minutes: in this way myocardial tissue could be characterized.
Results: 6 patients out of 8 with SVT presented an increased enhancement near the infundibular patch and in the anterior wall of right ventricle compared with 2 patients who had not history of SVT (p=0.03).
Conclusions: even if the number of our patients is small, there is a significant correlation between patients who present increased enhancement and history of SVT and those without SVT. The presence of late enhancement represents an area of fibrosis near the infundibular patch which is surely an arrhythmic surround for ventricular tachycardia.

Notes:

P28 Sino-tubular aorta dilatation in aortic valve disease: morphological analysis of medial changes.

S.Esposito, F.Ferraraccio, M.Accardo, P.Santé, M.Cotrufo, L.Cuccurullo, L.Agozzino; Naples-I

Background: To investigate whether and how the severity of medial degeneration lesions varies along the circumference of the dilated intrapericardial aorta.
Methods: Two groups of aortic wall specimens, respectively harvested in the convexity and concavity of ascending aorta in 72 patients undergoing surgery for dilatation of the intrapericardial aorta associated with aortic valve disease, were separately sent for pathology, morphometry and ultrastructural examination. Morphological changes found were classified in three degrees of severity; their mean degree and morphometric findings in the convexity and in the concavity specimens were compared by paired t-test. Correlation between echocardiographic degree of aortic dilatation and severity of medial degeneration was assessed separately for each of the 2 groups of specimens.
Results: Morphologically medial degeneration was found in all cases; a higher mean degree was found in the "convexity" group (2.39 ± 0.58 vs 1.44 ± 0.65 in the "concavity" group; $p<0.001$). At morphometry normal smooth muscle cells in the "convexity" specimens were significantly reduced ($p=0.007$); the length ($p=0.012$) and number ($p=0.009$) of elastic fibers reduced and increased respectively. Correlation between aortic ratio and medial degeneration degree was significant in the "convexity" ($p<0.001$), not in the "concavity" ($p=0.249$). Scanning electron microscopy analysis confirmed morpholgical results and allowed to better distinguish the pathological cavities from the microvessels which were in the outer media in normal aorta and ubiquitary in aortitis or atherosclerosis.
Conclusions: Medial degeneration changes in dilated intrapericardial aorta are more severe in the ascending aorta convexity, likely due to haemodynamic stress asymmetry.

Notes:

P29 Desmin-free cardiomyocytes and myocardial dysfunction in end stage heart failure.

S.Esposito, F.Ferraraccio, S.DiSomma, M.P.DiBenedetto, G.Salvatore, G.Caputo, O.DeDivitiis, L.Agozzino; Naples-I, Rome-I

Our aim was to evaluate the desmin content in the myocardial tissue of patients with end-stage heart failure of ischaemic origin and to assess its role on cardiac function. We studied 18 explanted hearts from patients transplanted for end-stage heart failure due to ischaemic cardiomyopathy (ICM). Control myocardial tissue was obtained from the cardiac biopsies of six women with breast cancer taken prior to commencing chemotherapy with anthracyclines, four male donors for heart transplantation and two autoptic hearts from patients who died due to non-cardiac events. Myocardial tissue, obtained from the left ventricle (remote zone from infarcted area), was analyzed by light and confocal immunochemistry (desmin) microscopy. The desmin content of myocardial tissue was obtained by real-time PCR. Cardiac function was evaluated by echocardiographic and right heart catheterization data, obtained before heart transplantation. Confocal microscopy evaluation showed a significant decrease in the number of desmin-positive myocytes ($P<0.01$) in ICM hearts compared to controls. At real-time PCR evaluation, there was a reduction ($P<0.01$) in desmin content in the ICM patients compared to controls. A negative correlation was found between desmin-free cardiomyocytes and ejection fraction (EF) ($r= -0.834$; $P<0.02$) on echocardiogram. A negative relationship ($r= -0.688$) was also found between desmin-negative myocytes and capillary wedge pressure. In conclusion, the myocardial tissue of patients with end-stage heart failure of ischaemic origin, shows a decreased number in desmin-positive myocytes at immunochemistry evaluation compared to normal individuals. This deficiency in cytoskeletal intermediate filament content is associated with reduced cardiac function.

Notes:

P30 Engraftment of extracardiac progenitor cells in an experimental model of heart transplantation.

T.Zaglia, E.Cozzi, A.Dedja, E.Ancona, S.Schiaffino, G.Thiene, S.Ausoni; Padua-I

Background: The ability of adult bone marrow (BM) stem cells to regenerate cardiomyocytes through transdifferentiation is a matter of intense debate. It has been reported that direct injection of BM cells into the infarcted myocardium induces regeneration through transdifferentiation. However, this observation has not been confirmed by recent studies. Extensive myocardial regeneration from extracardial progenitors in sex-mismatched heart transplantation has likewise been described, but subsequent studies reported only negligible contribution of stem cells to regeneration. In order to investigate the problem, we generated a model of eterotopic heart transplantation, to test the possibility that extracardiac stem cell progenitors from the recipient engraft into the donor heart and regenerate damaged myocardium.
Methods: Eterotopic heart transplantions (n=22) were performed between wildtype donor rats and transgenic recipient rats expressing the green fluorescent protein (GFP) ubiquitously. The transplanted hearts were removed after 15 (n=9), 30 (n=6) and 90 (n=7) days after surgery, fixed and processed for histology, immunohistochemisty and confocal image analysis.
Results: We observed multiple GFP-expressing cells in the transplanted hearts. Most of them were mature hematopoietic cells of the inflammatory and immune infiltrates. In 15/16 transplanted hearts, removed 15 and 90 days after surgery, we observed GFP+ cardiomyocytes with the typical morphology and protein profile of mature contractile cells, as shown by expression of lineage markers such as MHC, cardiac TnI and connexin 43. GFP+ cardiomyocytes were found in areas of tissue damage, always surrounded by healthy cardiomyocytes. These cells were present in small percentages, ranging from 0.0005 to 0.042% of all cardiomyocytes. Only in one heart we found endothelial GFP+ cells laid in the intima of large and small coronary vessels.
Conclusions: These results suggest that there is a spontaneous engraftment of host-derived progenitor cells into the transplanted hearts. These cells contribute to formation of GFP+ cardiomyocytes and endothelial cells, however this is a very rare event. Transdifferentiation versus cell fusion is currently under investigation using sex-mismatched transplants and FISH analysis.

Notes:

P31 Mutation screening of desmoplakin gene in 40 unrelated Italian index patients with a classical form of arrhythmogenic right ventricular cardiomyopathy.

G.Beffagna, A.Rampazzo, C.Basso, A.Nava, B.Bauce, G.Thiene, G.A.Danieli; Padua-I

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetically heterogeneous disorder associated with high risk of juvenile sudden death and characterized by extensive fibro-fatty replacement of right ventricular myocardium. Myocardial degeneration may involve left ventricle and, less frequently, inter-ventricular septum. Clinical manifestations of the disease include structural and functional abnormalities of the right ventricle, electrocardiographic depolarization/ repolarization changes and arrhythmias of right ventricular origin.
Eight autosomal dominant forms of ARVD, all exhibiting incomplete penetrance, were identified through linkage studies. Mutations in cardiac ryanodine receptor (RYR2) and in desmoplakin (DSP) were shown to cause ARVD2 or ARVD8, respectively.
In a previous study on one ARVD8 family, we first reported on identification of a causative mutation (S299R) in exon 7 of desmoplakin gene (DSP) Here we report on three additional novel mutations we recently detected and on the one previously described. We collected clinical data on 40 unrelated Italian index patients affected with a classical form of ARVD and of their family members. We performed a complete mutation screening of desmoplakin gene (DSP). Denaturing high performance liquid chromatography (DHPLC) and DNA direct sequencing succeeded in detecting the following mutations: c.423-1G>A; c.897C>G (p.S299R); c.3764G>A (p.R1255K), c.5324G>T (p.R1775H). One of the reported mutations (c.423-1G>A) was a heterozygous A>G transition at the acceptor site of intron 3 of the DSP, which results in an aberrant spliced mRNA. The predicted mutant DSP protein sequence contains only 200 aminoacids, due to the presence of a premature stop codon. Any of these nucleotide changes was found in 100 healthy control individuals obtained from the same population (200 chromosomes).
In two of the four ARVC families, episodes of juvenile sudden death were reported. In both cases autopsy was performed with a diagnosis a typical overt form of ARVC with fibro-fatty replacement of both ventricles in one, and a concealed form with subacute myocardial necrosis and early fibro-fatty substitution in the subepicardial layers of the left ventricular wall in the other.
It is interesting to notice that mutations in the desmoplakin gene (DSP), besides ARVD8, may underlie a dominant skin disorder without apparent cardiac involvement, a recessive condition characterized by dilated cardiomyopathy, woolly hair and keratoderma and a recessive condition characterized by arrhythmogenic right ventricular dysplasia, skin disorder and woolly hair.

Notes:

P32 Mutation screening of SCN5A gene in 35 index patients with Brugada syndrome.

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Background. The Brugada syndrome (BS) is a distinct form of idiopathic ventricular fibrillation and may cause sudden death in apparently healthy young individuals. Surface ECG abnormalities constitute the hallmark of Brugada syndrome, which includes ST segment elevation in the right precordial leads (V1-V3) associated with complete or incomplete right bundle branch block (RBBB), normal QT duration, and mild conduction defects with prolonged PR interval. *SCN5A (alpha-subunit of the cardiac sodium channel)* is the only disease-gene identified so far. The syndrome is inherited as autosomal dominant trait, with incomplete penetrance.
Material and methods Clinical investigation included complete physical examination, 12-lead electrocardiograph (ECG), echocardiogram (M-mode and two-dimensional) and Signal-Averaged Electrocardiography (SAECG). Mutation screening was conducted by a denaturing high-performance liquid chromatography (DHPLC) and by direct DNA sequencing
Results Here we report results of a mutation screening of SCN5A gene in 35 patients with Brugada syndrome. This series of index patients includes 18 familial and 17 isolated cases. Five novel *SCN5A* mutations (E473X, R814Q, del1775F, K1233X, F2004L) and one already described (E1225K) were found in cases with family history of juvenile sudden death.
A group of 150 healthy individuals randomly selected from the same population was used as control, in order to assess whether novel mutations detected in the *SCN5A* gene were polymorphic variants.
Conclusions. Our study shows that genetic screening in BS is more useful in familial than in isolated cases and it may be particularly helpful in early recognition of high-risk patients in a familial setting.

Notes:

P33 Detection of recipient origin cardiomyocytes in orthotopic heart transplantation.

C.Castellani, A.Angelini, M.DellaBarbera, M.Valente, A.Gambino, A.L.P.Caforio, G.Feltrin, G.Gerosa, G.Thiene; Padua-I

Background: The dogma of the myocardium as a permanent tissue it has been replaced by the concept that myocardium can regenerate, the cardiac myocytes can divided later in adulthood, that cardiac remodelling can be due to hyperplasia of stem cells. Cardiac chimerism offered the unique opportunity to recognize the formation of myocytes and vascular structure from primitive cells resident in the heart or homed to the heart from the circulation. Thus representing a self-repairing mechanism. Previous studies confirmed the existance of chimerism, namely colonization of donor female heart by male recipient cardiomyocytes, but gave a great discrepancy about magnitude and biological relevance of the phenomenon. An elegant approach to the assessment of this phenomenon is the use of fluorescence and the chromogenic in situ hybridization (FISH and CISH) for detection of Y-chromosome. Aim of our study was to evaluate the presence of chimerism and its kinetic over time.
Methods: Endomyocardial biopsies were obtained from the right ventricles of male patients (n=17, mean age 43,5± 23,9 years; range from 11 to 73) who had undergone sex-mismatched orthotopic heart transplantation. Five endomyocardial biopsies from non-transplanted male and non-transplanted female respectively served as controls. Cells from recipient origins were identified by in situ hybridization probe for Y-chromosome (CAMBIO, STAR-FISH™, UK, and VYSIS, USA) on paraffin sections of each biopsies. Rejection scores (according to a modification of ISHLT grading sistem) were calculated for all patients. Biopsies at 3 different time points were examined in all the patients. A total of 20.000 cardiomyocyte nuclei were analysed.
Results: Endomyocardial biopsies of non transplanted male showed a positivity for Y-chromosome in 47,51±1,40% of nuclei while non-transplanted female endomyocardial biopsies were always negative. Cardiomyocytes of recipient origin were detected in 88,23% of patients with a mean percentage of 0,20 ± 0,12% (in young patient: 0,35± 0,07%; in adult patients: 0,19±0,12%). Regression analysis showed a positive correlation between the Y-chromosome positive cardiomyocyte and the rejection index ($p<0.001$) suggesting that colonization could be more pronounced when cardiac injury is more severe. Y-chromosome positive cardiomyocytes were located as single cells and in area without fibrosis. There was an increase of recipient-derived cells in the donor hearts over time.
Conclusions: These results confirm that extracardiac progenitor cells were able to migrate into the myocardium or to differentiate in cardiac myocytes. The chimerism phenomenon seems to be influenced by graft survival time, age of the patients and by rejection index, all acting as stimulating factor, for the recruitment of stem cells.

Notes:

P34

P34 V.E.S.A.L.I.O. project.

F.DiMarco, B.Bertipaglia, G.Gerosa; Padua-I

The interest toward valve substitutes other than prostheses has stimulated cardiovascular research since the early seventies. In 1971, Dr. Alain Carpentier developed a collagen-derived heart valve with the aim to combine the excellent hemodynamics of valve grafts with durability of valve prostheses. The pioneering step of Dr. Carpentier opened the way to the future tissue engineering approaches.
During the last 6 years the V.E.S.A.L.I.O. (Vitalitate Exornatum Succedaneum Aorticum Labore Ingenioso Obtenibitur) project has been constituting the concrete form of the motivation of our group toward the creation of the ideal valve substitute. Our project is focused on 4 major issues:

1) to characterize cell composition of both aortic and pulmonary human valve
2) to develop decellularization methods to produce aortic and pulmonary scaffolds
3) to verify mechanical properties of aortic and pulmonary matrices
4) to identify the most appropriate cells and techniques to seed the matrices

We assessed cell population of human pulmonary valve comparing it with aortic valve, identifying three distinct phenotypes in both valves. We created aortic valve decellularized bioscaffolds and investigated the repopulation by cultured interstitial aortic valve cells. We observed that cultured interstitial cells repopulate the matrix giving rise to mesenchimal cells whose phenotype correspond to the native cell components of aortic valve. We applied refined technologies to produce decellularized matrices. Currently bone marrow stem cells, cordal blood and amniotic fluid cells are under investigation as alternative cell sources.
We are strongly convinced that nowadays regenerative medicine is no longer an option but a due way to pursue toward excellence.

Notes:

P35

P35 Pattern and distribution of fibrosis in the heart of patients dying suddenly of idiopathic cardiac fibrosis.

E.Reed, Y.Ho, M.N.Sheppard; London-UK

Primary restrictive cardiomyopathy is a myocardial disease of unknown etiology. Its pathophysiology as a true cardiomyopathy in questioned. It has a poor prognosis, particularly men >70 years old. Diffuse fibrosis of the ventricle is seen in many cases. We have studied 10 cases of idiopathic fibrosis of the left ventricle in patients who died suddenly. Extensive sampling of a transverse slice of the heart was done (7 blocks in each case). Tissue has been taken, fixed and stained for Picro-Sirius Red to detect collagen. The patients ranged in age from 11-67 years. 5 male, 5 female. Macroscopically the ventricles have a normal appearance with no dilatation or hypertrophy. The atria are not dilated and coronary arteries and valves are normal. Small macroscopic areas of scarring were noted in only 4 of the 10 cases. Microscopic analysis revealed widespread fibrosis both as large/small replacement fibrosis and perimyocyte/interstitial fibrosis in all cases. The distribution and pattern of fibrosis was very heterogenous with no specific zonal pattern. The haphazard distribution suggests that a myopathic/genetic mechanism is likely. This study emphasises that full histological analysis of the myocardium is essential to detect idiopathic cardiac fibrosis. The pattern of fibrosis is variable and is often more extensive than that detected by the naked eye.

Notes:

P36 Myocardial damage with head injury may mimic diffuse myocarditis.
F.MacSweeney, M.N.Sheppard; London-UK

Transmurally scattered foci of damaged myocardial fibres are reported significantly more common in patients with intracranial lesions compared to controls. Focal myocardial damage requires at least six hours to develop after onset of the acute neurological event and is not observed after the second week. Catecholamines have been implicated secondary to rapidly increasing intracranial pressure. 30 hearts removed from patients dying of head injury (used for valve homograft donation) were examined. Hearts appeared macroscopically normal with normal coronary arteries. It was noted that the myocyte damage with myocardial infiltration by lymphocytes, macrophages and some eosinophils and neutrophils was more frequent and diffuse than previously reported in 12 cases. These 12 cases ranged in age from 23-57 years, 7 males, 5 females. The inflammation was not just around individual myocytes but also in the interstitium. The pattern was heterogenous with some areas showing focal small changes while other areas of the ventricle showed widespread changes in individual patients. No relation to type of head injury was noted. Immunostaining for CD3 and CD68 showed large numbers of T lymphocytes and macrophages mimicking myocarditis.
Pathologists need to be aware of these changes in autopsy studies of head injury and sudden death.

Notes:

P37 Pathology of surgically removed cardiac valves in a specialist UK Center.
M.Gudi, M.N.Sheppard; London-UK

The incidence of valve heart diseases differs according to many factors including age, geography and infection. We analysed the last decade of surgically removed valves at our hospital. In this period, 1500 valves were removed. Aortic valve numbered (864), Mitral valve (411), Tricuspid valve (8) and Pulmonary Valve (6). Also included were bioprosthetic (20), mechanical (5) and homograft valves (155). There were (894) males and 606 females. The younger patients had congenital valve disease including congenital mitral stenosis (6), bicuspid aortic valve (195), congenital supraortic stenosis (1), congenital subaortic stenosis (20). Pulmonary valve stenosis (usually associated with Fallots Tetralogy (4). Tricuspid valve Ebsteins anomaly (2). Acquired disease included predominantly aortic stenosis due to degenerative calcification (378), rheumatic disease (246), floppy mitral valve (240), including (12) associated with Marfans syndrome and mitral stenosis due to rheumatic disease (145). Bacterial endocarditis of aortic valve (40) and mitral valve (20). Other causes of aortic and mitral valve regurgitation included connective tissue disease (8). Valve replacement included bioprosthetic valve degeneration (20), mechanical valves (5) and degenerate homografts (137). The older population reflects degenerative disease of both aortic and mitral valve in this study. Congenital disease is also significant in view of referral pattern as well as valve replacements. Rheumatic disease is much less than in previous decades.

Notes:

P38 New anticalcification treatments of glutaraldehyde fixed bovine pericardium in the subcutaneous rat model.

E.Pettenazzo, G.Thiene, M.Valente; Padua-I

Background. The main anti-calcification strategies, nowadays available in glutaraldehyde (GA) fixed xenograft tissue, aim to lipid extraction, thus removing the potential sites of calcification, or to neutralization of free toxic aldehyde residuals. The aim of this study was to evaluate the efficacy of two anticalcification treatments, Homocysteic acid (HA) and 1,2-octanediol (ON), of GA fixed bovine pericardium (BP), whether isolated or in association (ONHA), and compared to standard GA fixed pericardium (ST). HA neutralizes GA toxicity by bonding aldehyde group residuals from cross-linking. ON treatment is a combination of 5% 1,2-octanediol in an ethanolic solution which should remove lipids and excess of GA as well.
Methods. Four squares of BP were implanted in each of 48 Sprague Dawley rats and explanted after 30 and 75 days (24 animals each). A total of 4 different combination were tested. The explants were fixed in formalyn, submitted to X-ray evaluation, and to morphological evaluation (histology, transmission and scanning electron microscopy). The parameters evaluated at histology were: presence, amount (score 0-4) and type of mineralization, collagen preservation, and presence, amount (score 0-4) and type of inflammatory reaction.
Results. The table summarizes the main findings. At 30 days a sharp difference was noted in terms of mineralization: BP treated with ON, and BP treated with ONHA both disclosed absent calcification. This trend was confirmed at 75 days. The collagen appeared well preserved in all cases, regardless the type of treatment. Calcific deposits involved both cells and collagen fibers.

Treatment Method	Mean calcification score		Mean inflammatory score	
	30 days	75 days	30 days	75 days
ST	3.2 ± 1.1	3.6 ± 0.7	2.2 ± 0.4	2.1 ± 0.9
HA	3.1 ±1.3	3.5 ± 1.2	2.5 ± 0.7	1.7 ± 0.6
ON	0	0.3 ± 0.9	2.6 ± 0.5	2 ± 0.6
ONHA	0	0	2.5 ± 0.5	1.9 ± 0.7

Conclusions. Treatments with ON and ONHA significantly mitigated BP calcification in rat subdermal model even in the long term. No differences in terms of tissue preservation were observed between the various treatments.

Notes:

P39 Desmosomes in arrhythmogenic right ventricular cardiomyopathy: an ultrastructural investigation of intercalated discs on endomyocardial biopsy.

M.DellaBarbera, C.Basso, M.Valente, E.Wlodarska, B.Bauce, A.Rampazzo, G.Thiene, C.Czarnowska; Padua-I, Warsaw-PL

Background. Mutations of genes encoding intercalated disc (ID) proteins, ie plakoglobin and desmoplakin, have been found to account for both autosomal recessive and dominant inherited forms of arrhythmogenic right ventricular cardiomyopathy (ARVC). Both proteins are constituents of desmosome (D) that links the intermediate filaments network and play an important role in maintaining myocardial integrity under mechanical stress. Thus D abnormalities have been postulated to represent an ultrastructural marker of ARVC.
Material and Methods. 21 patients (10 M and 11 F, mean age 24,5±14 yrs) with an in vivo diagnosis of ARVC according to the task force criteria underwent right ventricular endomyocardial biopsy (EMB). Familiarity was present in 8 (38%). Ten EMBs from donor hearts for cardiac transplantation served as controls. EMB samples were fixed in Karnowsky/osmium tetroxide, embedded in Epon 812 and observed under a Hitachi electron microscope. IDs were evaluated in terms of convolution index, D and nexus length (micron), D and nexus percent ID length, and D and nexus number per ID unity length (10 micron). Moreover, D gap size and internal and external plaques were assessed.
Results. No major differences were found in terms of convolution index in ARVC vs controls (2,9 vs 2,9, p=NS). Mean D length and the percent D/ID length were higher, in ARVC as compared to controls (0,32±0,17 vs 0,14 ± 0,08; 10% vs 5%) and the D number /ID unity length was lower than in controls (3,38±1.47vs 5,54 ± 3,06) with all p value <0.01. In ARVC, 75% presented abnormally located D and 32% pale internal plaques. In ARVC Nexus was observed at ID more rarely than in controls (21% vs 75%) while D and fascia adherents (FA) were wider than controls (29,33 ± 8,95 vs 21,68 ± 3,42, p=0,004; 41,49 ± 20,36 vs 27,18 ± 10, 62, p=0,03) respectively, with no difference in nexus gap (16, 08 ± 3,04 vs 15,20 ± 3). No correlation was found between age and any of the ultrastructural parameters investigated.
Conclusions. ARVC shows at ultrastructural level D abnormalities consisting of increased D length and decreased D and nexus number and D and FA gap widening in the absence of ID convolution changes.. Genotype-phenotype correlation is warranted in order to establish differences among ARVC pts with and without gene mutations encoding D proteins.

Notes:

P40

P40 Cardiac amyloidosis – myocardial biopsy diagnosis.

D.Butcovan, C.Arsenescu, C.Borza, D.Pintilie, G.I.M.Georgescu; Iasi-RO

The paper evidentiates the morphoclinical picture in cardiac amyloidosis to a 50 years old man admitted at Iaşi, Cardiology Center (CCI) with progressive chronic cardiac failure, the patient having recent history of restrictive cardiomyopathy (RMC). It was made a complete cardiovascular evaluation including the right cardiac catheterization for endomzocardial biopsy (EBM). The byopsic specimens were fixed in buffered 10 % formalin, followed by routine paraffin embedding, and were stained with haematoxylin-eosin (HE), elastic Van Gieson (EVG) and sulfated Alcian blue (AAS) for amyloid evaluation. The amyloid deposits, evidentiated in the interstitium and into vascular walls on the biopsy, pointed the importance of the morphological exam for amyloidosis diagnosis.

Notes:

P41

P41 Tracheal aspirate a sensitive method for viral detection and tumor necrosis factor alpha in pediatric myocarditis.

Y.Kato, Y.Kato, E.Carturan, F.Calabrese, O.Milanesi, G.Thiene; Padua-I, Toyoake-J

Background: Pediatric myocarditis is a serious disease resulting in significant morbidity and mortality. Endomyocardial biopsy, the best tool for final diagnosis of myocarditis, has been considered an unsafe procedure and of low diagnostic yield in children. Recently tracheal aspirate (TA) has been demonstrated a sensitive diagnostic tool for detection viral infective agents responsible of respiratory disorders and myocardial dysfunction. Tumor necrosis factor (TNF) alpha (a) has been found to play an important role in the pathogenesis and pathophysiology of these disorders, particularly of inflammatory cardiomyopathy. The aim of present study is to investigate the presence of different types of viruses and expression of TNFa in TA from children with clinical suspicion of myocarditis.
Methods: Thirty-seven TA from children (16M/21F, mean age 4.5 ± 5.2 year) with respiratory disorder and myocardial dysfunction were collected in our Institution from January 2001 to August 2004. All TA were analysed for detection of cardiotropic viral genomes and TNFa expression (mRNA) by using PCR and RT-PCR. The quantification of transcript level was carried out with densitometric analysis. TNFa protein plasma levels were assessed by ELISA. Molecular data were correlated with all clinical and serological data.
Results: Viral etiology was detected in 22 cases: Enterovirus 9, Herpes Simplex virus 4, Enterovirus/Cytomegalovirus 2, Adenovirus 2, Epstein-Barr virus 1, Parvovirus B19/Cytomegalovirus 1, Cytomegalovirus 1, Adenovirus/Enterovirus 1 Adenovirus/Enterovirus/Cytomegalovirus 1. Densitometric analysis revealed that the mRNA levels for TNFa were significantly over-expressed in viral cases (1,63 vs 0,66 p=0.01). In the viral cases TNFa serum levels were also over-expressed (15.78 vs 3.33 p=0.008). We have observed that TNFa positive cases show a more impaired cardiac function than TNFa negative cases, particularly evident for ejection fraction (cut-off value: 55%) (TNFa positive vs TNFa negative, p=0.04) and cardio-thoracic ratio (cut-off value: 50%) (TNFa positive vs TNFa negative, p=0.02).
Conclusion: TA appears to be an excellent analysis to investigate etiology and pathogenesis of myocarditis in pediatric population. Virus is a frequent cause of myocardits and respiratory disease. The over-expression of TNFa in viral cases may play a key role in the pathogenesis of myocardial dysfunction. TNFa may be considered a pivotal parameter for prediction of cardiac function.

Notes:

P42

P42 Outcome of patients with severe form of arrhythmogenic right ventricular cardiomyopathy/dysplasia.

G.Frigo, B.Bauce, L.Daliento, C.Basso, A.Nava; Padua-I

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a myocardial disease characterized by right ventricular abnormalities and life-threatening ventricular arrhythmias. The natural history usually considers a "concealed" phase and a period of "overt electrical disorder", followed in some cases by a severe right ventricular dysfunction and by a biventricular pump failure. However, published studied did never focus on the clinical features and follow-up of patients with a severe form of the disease in terms of right ventricular morphological alterations.
In the present study a total of 18 consecutive subjects (15 males, 3 females, mean age 33±15 years) with severe ARVC/D were studied with a follow-up programme. At the time of the beginning of the study nine patients have already experienced an episode of life-threatening ventricular arrhythmias (sustained ventricular tachycardia-VT- or ventricular fibrillation). During follow-up (max 20, min 2, mean 11±6 yrs) 12-lead ECC, signal-averaged ECG and 2D-echocardiogram did not show significant changes. Eight patients experienced further major cardiovascular events, consisting in sustained VT episodes in 6 (in two of them this was the first documented VT episode) and heart failure in 2 (one of these died due to stroke). One patient underwent heart transplant due to recurrent sustained VT episodes with ICD shocks.
In conclusion patients diagnosed with a severe form of ARVC did not show significant changes of instrumental parameters, in contrast with a high incidence of cardiovascular events. These data confirm that in ARVC/D the extent of the disease is an important parameter for the arrhythmic risk stratification.

Notes:

P43

P43 Concealed arrhythmogenic right ventricular cardiomyopathy: pathologic substrates and high resolution MRI.

E.Maresi, L.Russo, R.Midulla, E.Orlando, G.Fazio, A.Pepe, M.Midiri, M.Lombardi, P.Procaccianti; Palermo-I, Pisa-I

Aim To evaluate the anatomo-pathological findings in a series of concealed ARVC/D and to correlate the anatomical patterns with those detectable by high resolution Magnetic Resonance Imaging (MRI).
Materials and Methods From January 1987 to May 2003, we performed 262 autopsies of USCD. In this series, ARVC/D group accounted for 20 cases (7.6 %), including 14 males and 6 females (16 to 43 years old; median 26 years). Circumstances of death were during physical exercise in 14 cases and at rest in 6 cases. The family history of ARVC/D and/or sudden death was negative.
Results The transmural loss of the myocardium in the right ventricular free wall was diffuse in 8 cases and segmental in 12 cases. External bulging of right ventricular free wall and left ventricular was present in 4 e 6 cases, respectively. The myocardial atrophy was replaced by fatty tissue in 13 cases (65%) and by fibro-fatty tissue in 7 cases (35%). The interface between residual cardiomyocytes and tissue replacing the myocardium (fatty or fibro-fatty) was wavefront (cardiomyopatic pattern) in 15 cases (75%) and lacelike (infiltrative pattern) in 5 cases (25%). Active myocarditis was detectable in the fibro-fatty variant only. MRI described the fatty replacement on T1-weighted images with moderate inter-intra observer variability, thus sequences like "fat suppression" or "triple inversion recovery" to evaluate fatty replacement might provide a significant improvement in the diagnosis of ARVC/D.
Conclusions Our data showed highly frequent association between concealed ARVC/D and the fatty variant with cardiomyopatic pattern. MRI is more sensitive to detect the fatty variant with the cardiomyopatic pattern rather than fibro-fatty and/or infiltrative substrate.

Notes:

CONTRIBUTORS

CONTRIBUTORS