招待講演・教育講演

L-1　招待講演 1　Marfan Syndrome

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Classical Marfan syndrome (MFS1) is a generalized connective tissue disorder caused by mutations in the fibrillin 1 gene. Marfan syndrome type II is caused by mutations in the TGFBR2 gene. In 1996 the revised "Ghent criteria" were offered as an international standard for the diagnosis of MFS. In 2010 these criteria have been revised. MFS is a hazardous condition, often associated with premature cardiovascular death unless surveillance and management are optimized.

The prognosis for patients with MFS mainly depends on the severity of cardiovascular complications. Particularly the neonatal form is often associated with a dismal course and with premature death. Progressive tricuspid and mitral valve regurgitation from atrioventricular valve prolapse are main causes of morbidity during infancy. Aortic ectasia, aortic dissection and chronic aortic valve regurgitation is the foremost cause of mortality and morbidity in adults. Aortic root abnormalities predispose to progressive aortic dilatation and dissection, aortic- and AV-valve anomalies to congestive heart failure. Aortic rupture, aortic dissection, and heart failure account for approximately 90 % of all deaths in adults.

Prior to adequate pharmacologic and surgical treatment the historically reported life expectancy of Marfan patients was about two-thirds of that of healthy people. The lack of diagnostic criteria and awareness of MFS with subsequent misdiagnosis were the main reason for high morbidity and mortality in the past. Over the past 4-5 decades, modern therapeutic concepts have considerably improved long-term outcome. Particularly, successful and timely aortic root surgery, aortic valve and mitral valve replacement or repair as well as earlier detection, careful follow-up and the prophylactic use of beta-blockers have reduced morbidity and mortality and prolonged survival. Nevertheless, cardiovascular complications are still the most common causes of patient loss, often due to sudden death in previously undiagnosed patients and in patients with rapid progression of previously diagnosed problems.

Diagnostic imaging

Diagnostic imaging is very important for detection and evaluation of cardiovascular involvement and case management, particularly to define therapeutic strategies.There is no single definite test modality for the diagnosis of MFS. In addition to a history of symptoms the family history and a complete, systematic evaluation of all potentially involved organ systems is mandatory, particularly regarding the heart and blood vessels, the eyes, and the musculo-skeletal system. In the past decade imaging modalities have shifted toward the use minimal invasive and noninvasive techniques. Doppler-echocardiography, magnetic resonance imaging (MRI), and modern computed tomography (CT) are the gold standard and should be judged as complementary in patients with MFS.

Management

Patients must be well informed about potential complications from the syndrome and how life-style modification can improve outcome. Guidelines for physical activity depend on the severity of the disease and the symptoms. Strenuous exercise, maximal and isometric exercises should be refrained. There is some evidence that beta-blocking agents prevent or delay the onset and rate of aortic root enlargement, reduce the risk of rupture or dissection and improve survival rate in all age group. The use of beta-blockers in MFS was established 1994 by a small prospective, open-label, randomized trial. Other retrospective studies confirmed the efficacy of beta-adrenergic blockade in patients with MFS. However, it is well known that some patients respond better than others do. Particularly from the pediatric group questions were raised, about the beneficial prophylactic effect.

Currently, all (adult) Marfan patients should be maintained on long-term beta-adrenergic blockade provided no contraindications exist. In the future, angiotensin converting enzyme inhibitors may play the most important roll in the prevention and treatment of aortic wall degeneration and disproportionate growth rate of the aortic root.

Cardiovascular surgery

Elective surgery is performed in adults to prevent aortic dissection or rupture or to treat aortic valve or AV-valve regurgitation. The indication for elective surgery is particularly based on aortic size, rate of aortic growth, and family history of aortic dissection. Prophylactic aortic root replacement is usually recommended when the diameter reaches 50 mm. However, certain experienced institutions replace the ascending aorta in adults as soon as the aortic root diameter exceeds 45 mm. Early aortic surgery is also recommended if the aortic root diameter is enlarging rapidly. Elective surgery can be indicated in patients with a family history of aortic dissection or sudden cardiovascular death even much earlier to avoid a disaster. Dissection of the descending aorta can usually be managed medically. The descending aorta should be replaced if the aortic diameter exceeds 55 or 60 mm, if complications, pain or organ ischemia is present, if the aortic diameter increases more than 0.5 to 1.0 cm per year, or when the aortic diameter exceeds twice the diameter of the normal aorta.

For infants and children no authoritative recommendations exist. Aortic surgery is performed as Composite Valve Graft repair (so-called modified Bentall procedure) or as valve-sparing aortic surgical repair. The Yacoub procedure is referred to as the "remodeling technique," and the David procedure as the "reimplantation technique" .

Recently, implantation of aortic stent grafts into the descending aorta was introduced for type B dissection in Marfan patients which could not be managed conservatively. However, the complication rate in MFS is significant and MFS patients are not ideal candidates for this procedure.

It has to be emphasized that Marfan patients receive their ongoing medical care at a subspeciality center. Surgery in MFS should only be performed by cardiac surgeons with special expertise and in experienced cardiac centers. After surgery Marfan-patients require lifelong follow-up to detect future progression of the disease in time. Particularly the aortic arch and the descending aorta are at risk for later-onset aneurysmal formation and dissection. The proposed control interval should not exceed 12 months in untreated patients with an aortic root diameter under 40 mm or in pts with an uneventful postoperative or postinterventional course. Patients with an aortic root diameter above 40 mm, with aortic regurgitation, after surgical or interventional treatment of the aorta, or with a family history of aortic dissection or sudden cardiac death should be restudied by echocardiography, with CT or MRI at least every 6 (to 12) months, as changes can occur suddenly, even in asymptomatic patients. Each MFS patient with new onset of acute thoracic or abdominal pain or with other extraordinary symptoms should immediately seek medical attention and urge for medical clarification, including imaging of the aorta.

L-2　招待講演 2　Doppler Echocardiography and Heart Failure in Congenital Heart Disease

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1. Introduction

Echocardiographic assessment of myocardial function is essential in patient with congenital heart disease, and patients with heart failure in particular. Evaluation of systolic function is challenging due to the confounding effect of many factors: ventricular geometry, variable loading conditions (pre-/afterload) and intrinsic myocardial function. Physiologic concepts of myocardial function and limitations of the different echocardiographic techniques must be understood.

2. Mechanics of Cardiac Systolic Function

Systolic function itself consists of intrinsic myocardial function (contractility) and ventricular pump function (performance). Ventricular performance further depends on many factors: ventricular geometry, loading conditions (venous return, valvular function, arterial impedance), myocardial perfusion, and heart rate. The stroke volume/cardiac output depends on: preload, afterload, heart rate and intrinsic contractility. The latter refers to the ability of the cardiac muscle to generate force and shorten independently of preload, afterload and heart rate. Most indices of cardiac function are indices of intrinsic contractility, but are also responsive to loading conditions and do not provide an accurate measurement of contractile function of the myocardium. The reference method for assessing ventricular contractility is the invasive recording of pressure-volume loops.

3. Echocardiographic Assessment of Ventricular Systolic Function

Different techniques were introduced to assess ventricular global or regional myocardial function.

a) Dimensional Changes To Assess Ventricular Function:

The following three measurements are used to assess global ventricular function:

- **Fractional shortening** (M-mode): to assess circumferential/radial shortening
- **Displacement of the atrio-ventricular valve annulus** – to assess longitudinal function (TAPSE: Tricuspid Annular Plane Systolic Excursion by M-mode; MAPSE: Mitral Annular Plane Systolic Excursion). Advantage: simple measurement, less dependent on optimal image quality. Disadvantage: assumption that the displacement of a single segment represents the function of a complex 3D structure, angle dependency, load dependency
- **Ejection fraction** (2 D–echocardiography, 3-D echocardiography). There are several challenges to calculate ejection fraction, in particular for the RV or in patients with univentricular hearts: abnormal geometry of the RV / univentricular hearts (geometrical assumptions); suboptimal/poor endocardial delineation/extensive trabeculations of the RV (how do you trace the RV volume? Do you include the trabeculae into the blood pool?) Calculation of the ejection fraction by 2 D echocardiography is not possible for the right ventricle (complex geometry). Three D-echocardiography is used to calculate RV ejection fraction.

- **Fractional area change (fac):** fac = (end-diastolic area – end-systolic area)/end-diastolic area.
- **Velocity of circumferential fiber shortening (VcF):** fractional shortening (FS) is divided by ejection time. This index is relatively insensitive to preload changes, but highly sensitive to changes in contractility and afterload. Limitations: global parameter; short-axis has to be circular and LV shape elliptical.

All these methods have limitations but they are commonly used in daily clinical practice (except VcF). As discussed, geometry and load dependency are one of their main limitations.

b) Doppler Measurements:

- **Maximal dP/dt:** The maximal rate of rise in ventricular pressure during the isovolumic contraction period (dp/dtmax) is an invasive index derived from pressure traces and reflecting pressure-generating capacity of the cardiac muscle. It can be derived from a continuous-wave Doppler tracing of AV valve regurgitation jet (there is no significant rise in left atrial pressure and therefore the rise in AV regurgitation velocity during isovolumetric contraction period reflects dP/dtmax). Limitation: dP/dt is not a real isovolumetric measurement because some volume changes in the ventricle are required for the regurgitant volume; preload-dependency; lack of data in normal subjects (dp/dtmax not recommended for routine use)s. Advantage: geometry-independent measurement and sensitivity to changes in contractility, relative independence from changes in afterload (measurements are performed before opening of the aortic valve).
- **Aortic/pulmonary blood flow velocities**
- **Myocardial Performance Index (MPI):** this is a non-geometrical index expressing global ventricular function (systolic and diastolic function). It includes isovolumic contraction time (ICT), ejection time (ET) and isovolumic relaxation time (IRT). MPI = (ICT + IRT) / ET. Normal values: 0.35 ± 0.03 for the left ventricle, 0.28 ± 0.04 for the right ventricle. The larger the MPI, the more abnormal ventricular function. Advantages: no geometric assumptions. Disadvantages: measure of global myocardial function; no differentiation between systolic and diastolic dysfunction, load-dependency; unreliable in patients with elevated atrial pressure.
- **Doppler Tissue Imaging (DTI):** It allows non-geometric quantitative measures of both systolic and diastolic ventricular function that is easily obtained, reproducible and clinically valid. DTI is a direct assessment of myocardial function (in contrast, the previously discussed measures of myocardial function by looking at dimensional changes or at blood pool data during the ejection period). The normal pulsed-wave DTI is characterized by first a short and sharp isovolumic contraction peak (S-wave), followed by a longer systolic contraction peak, that corresponds to base-to-apex motion of the myocardium during systole. This is followed by another short-lived isovolumic relaxation peak. Later, the early diastolic (E-wave) and the late-diastolic waves (A-wave) occur. Limitations: dependency on heart rate, age, geometry, preload, afterload and angle; tissue Doppler velocities also are unidimensional and rely on a one-dimensional assessment of the myocardial velocity (in either the longitudinal or radial direction); cardiac translation (movement of the heart within the thorax) is also measured; in addition, motion and velocity of a myocardial segment are influenced not only by its own intrinsic contractility but also by adjacent myocardial segments (defined as tethering). Advantage and disadvantage: the same as displacement atrio-ventricular annulus; plus segment interaction.

- **Myocardial acceleration during isovolumic contraction (IVA):** this is an index of contractility calculated as the average rage of myocardial acceleration during isovolumic contraction and expressed in centimeters per second. IVA has been validated as a sensitive noninvasive index of right and left ventricular contractility that is unaffected by preload and afterload within a physiologic range. Limitations: heart rate dependent; preload dependent in patients with elevated ventricular EDP, no consistent relationship between regional IVA and regional myocardial contractility in patients with ischemic heart segments. IVA should only be used as global functional parameter when calculated from longitudinal velocities near the base of the heart.

b) Doppler Measurements:

- **Strain and strain rate:** to assess regional deformation. Limitations: angle-dependent and load-dependent technique; no clinical validation/lack of normative data. Research tool; segment interaction.
- **Speckle tracking:** IAngle-independent. Limitation: load-dependent; very limited clinical use

4. Echocardiographic Assessment of Diastolic Function

Diastolic function/dysfunction has been less well understood and investigated than systolic function. One of the major challenges are that Doppler patterns that characterize diastolic function vary significantly among different congenital heart defects and are not validated at all. All normal values of diastolic indices obtained and validated in adults with normal structure of the heart or acquired heart disease canNOT be extrapolated and applied to patients with congenital heart disease. What are normal diastolic indices for a subaortic right ventricle or a univentricular heart (Fontan circulation)? There is a lack of validated data.

a) Doppler echocardiography: mitral/pulmonary venous inflow; tricuspid/systemic venous inflow; pulmonary venous inflow

b) Tissue Doppler Imaging (TDI): Pused TDI can be useful, but there are limitations: angle-dependency; it is critical to interrogate the myocardial segment parallel to the wall motion in order to obtain true peak velocities; segmental wall motion patterns do not reflect global myocardial function.

c) Myocardial deformation:

- strain/strain rate. Limitations as discussed above.
- Speckle tracking

d) Atrial volume(s): it reflects chronic cumulative filling pressures over time (in contrast to Doppler indices, which describe diastolic function at one moment in time).

e) Inferior vena cava: dimension and respiratory variation

5. What Can/Should I Measure During My Daily Clinical Practice?

Be aware of the limitations of each method!

a) Systolic function:

- Visual assessment
- Fractional shortening
- Fractional area change
- Ejection fraction (left ventricle); it may be reasonable to reserve 3 D echocardiography to calculate volumes/ejection fraction in selected patients (right ventricle, univentricular heart?) and laboratories

- Displacement of the atrio-ventricular valve annulus (TAPSE/MAPSE)
- DTI at the base of the ventricles (S')
- (MPI – measure of global ventricular function)

Diastolic function:

- Tricuspid/systemic venous inflow
- Mitral/pulmonary venous inflow
- DTI at the base of the ventricles
- Atrial volume(s) / inferior vena cava (IVC)
- (MPI – measure of global ventricular function)

The following parameters are **research tools:**

- Strain/strain rate; speckle tracking
- IVA

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6. Summary

- There is no single, robust technique available to measure systolic / diastolic function of the ventricles in patients with (complex) congenital heart disease.
- isual assessment of systolic ventricular function is inadequate and quantitative parameters must be routinely obtained; at least two, reproducible parameters of systolic and diastolic function must be incorporated into the routine echocardiographic assessment of the ventricle(s) . Combining more than one measure of ventricular function is more reliable;
- Normal values derived from healthy subjects/patients with acquired heart disease cannot be extrapolated and applied to patients with congenital heart disease; each patients is his/her own control during follow-up;
- **Longitudinal data and dynamic changes** of the measurements are more important than one single measurement;
- All methods have major limitations including load-dependency, heart rate dependency and/or geometry-dependency.

LS　ランチョンセミナー

チーム医療に欠かせない情報ネットワーク構築と心臓超音波診断の取り組み

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多職種が診療記録・検査情報・画像情報（静止画と動画）情報を共有して活用できることは，成人先天性心疾患の診療に大変役立つことを実感しています．今回，当院で行ってきた情報ネットワーク構築の取り組みをご紹介いたします．また，先天性心疾患の診断と病態の把握に欠かせない超音波検査への取り組みもご紹介させていただきます．

１．情報ネットワーク構築と運用への取り組み

２００７年までは，放射線室･心臓カテーテル室･超音波検査室といった部署単位でシステムを順次導入した結果，放射線画像（静止画）・心臓カテーテル画像（動画）・超音波画像（静止画と動画）の3つのシステム構成となり，同一患者さんのデータを参照するには3台の端末で各々検索表示する必要があり業務効率は低いにもかかわらず投資額は大きかった．２００８年にGoodnetの動画PACSを導入して，心臓カテーテル検査画像および超音波の静止画と動画像データを一元管理に変更した．小児循環器の解析にはカテックスのシステムを用いているが画像連携により省力化も実現できた．さらに中央検査室のすべての超音波検査機器および手術室・新生児NICU・ICUで取得された超音波画像が，DICOMサーバーに集約されている．報告書は，柔軟に変更可能なファイルメーカーで作成してPDF形式で確定保存できる．このシステムでは，関連する心カテ履歴一覧や心エコー検査一覧，報告書一覧をワンクリックで表示することが可能で作業効率は極めて高い．また，富士メディカルの放射線画像システムであるSynapseとも連携しており放射線画像やレポート一覧もワンクリックで表示可能である．２００９年にNEC社製電子カルテMegaOakHRの導入によりGoodnetシステムと富士メディカルのシステムを電子カルテ上から利用できるようになっただけではなく，１９９４年から電子保存されている心電図情報や２００７年から電子化されている退院時要約の表示なども可能となっており患者像の把握が容易になった．

２．成人先天性心疾患の病態の把握に欠かせない経食道心エコーの技術伝達の取り組み

当院では，最初に循環器内科の医師ができるようになり，次に麻酔科の医師と勉強会を重ね一緒に取り組むことで麻酔科医への技術と判断の伝達ができた．さらに，心房中隔欠損症をディバイスで閉鎖する時に経食道心エコーが欠かせませんので小児循環器の医師を支援して独り立ちできるようになった．また，3Dエコーの画像取り込みと解析ができる熟練した超音波検査士の育成も行った．これらの取り組みをご紹介します．

３．先天性心疾患で欠かせない血流情報の可視化と定量化の取り組み

最後に，これまで形態診断について素晴らしい進歩がありますが血流の可視化と定量化については立ち遅れていました．しかしながら東京工業大学名誉教授の大槻茂雄先生と東北大学名誉教授の田中元直先生が取り組まれているEcho-Dynamographyの開発により様々な進歩が期待できるのでこの技術がもたらす展望をご紹介いたします．

MS　モーニングセミナー
心臓 CT 検査にともなう放射線被曝リスクの評価

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心臓 CT 検査は，近年先天性心疾患患者に対しても広く普及してきた．小児から若年成人期にかけては放射線感受性の高さから中高年患者とは異なった配慮が求められる．検査に関わる医療従事者は，この検査に伴う放射線被曝リスクについて基本的な知識と正しい理解を持つことが重要である．とくに，成人期先天性心疾患患者を対象とした場合，人生の早期に治療的介入を行って，心血管系の何らかの遺残症や中長期において発生する合併症を監視，発見することが多く求められるため，かなりの長期にわたり繰り返し検査を施行することを前提に，検査方法やプロトコールの選択，設計をすることが必要である．

心臓 CT 検査では装置やプロトコールの選択により侵襲的カテーテル検査と同等かそれ以上の被曝になり得るため，被曝の問題を避けて通ることはできない．一方で，最新の装置や撮像方法によれば小児心臓 CT における被曝線量は約 0.25 mSv（胸部単純 X 線写真の５枚程度）にまで抑制しうるという報告もなされるようになった．

心臓 CT 検査に伴う放射線被曝リスクについては，臨床的にバランスのとれた考え方をすることが大切である．そのためには，以下の複眼視的な観点，すなわち，1）患者被曝線量，および被曝に伴う生物学的リスクを推定する原理，ならびにこれら推定値の不確実さに関する理解，2）放射線被曝および他の原因による発がんリスク強度の比較，3）被曝の危険性を畏れて検査を忌避することで，重要な診断や治療の決定が遅れるか行われないための不利益や危険性の認識，が必要である．

本講演では，放射線被曝を伴う心臓 CT 検査を小児，若年成人において安全に施行するための考え方の枠組みを提供する．同時に心臓 CT が有用とおもわれる心血管形態異常の具体例についても提示する予定である．