Report

Meeting Report: Heart Failure 2010.

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Heart failure is defined as the inability of the heart to supply sufficient blood flow to meet the rigorous demands of body [1]. It is a global term for the physiological state in which cardiac output is insufficient for the body's needs. It occurs most commonly when the cardiac output is low and is also known as "congestive heart failure" (CHF) because the body becomes congested with fluid. Over time, conditions such as coronary artery disease or high blood pressure gradually leave the heart too weak or stiff to fill and pump efficiently [2]. The term 'heart failure' is often used incorrectly to describe other cardiac illnesses, such as heart attacks (myocardial infarction) and cardiac arrest. Heart failure is a common, costly, disabling and potentially deadly condition. It is an especially important problem in the elderly (Jugdutt, 2010). Around 2% of adults suffer from heart failure in developing countries, but in those over the age of 65, this increases to 6–10%. The disease is associated with significantly reduced physical and mental health, resulting in a markedly decreased quality of life. With the exception of heart failure caused by reversible conditions, the condition usually worsens with time. Although some patients survive many years, progressive disease is associated with an overall annual mortality rate of 10%.

Heart failure presents a serious challenge to the health authorities because of the high health expenditure associated with treating patients. In the United Kingdom alone 2% of the total budget of the National Health Service in the United Kingdom is spent on heart failure patients. The figure is much larger in the United States, around $35 billion in the United States.

Common causes of heart failure include myocardial infarction (heart attacks) and other forms of ischemic heart disease, hypertension, valvular heart disease and cardiomyopathy. The rise in diabetes, hypertension and obesity has resulted in increased cases of heart failure. Heart failure can cause a large variety of symptoms such as shortness of breath and exercise intolerance. Heart failure is often undiagnosed due to a lack of a universally agreed definition and challenges in definitive diagnosis. Treatment consists of lifestyle measures (such as weight control and decreased salt intake) and medications, and sometimes devices or even surgery.

Personalized management of heart failure can be considered across the entire spectrum of this disease, from monogenic disorders, to modifier genes and pharmacogenomics (Mestroni et al., 2010). Monogenic disorders that cause heart failure are the cardiomyopathies. In this

[1] http://www.heart.org/HEARTORG/Conditions/HeartFailure/Heart-Failure_UCM_002019_SubHomePage.jsp

[2] http://www.mayoclinic.com/health/heart-failure/DS00061

disease, recent guidelines have been introduced to assist the clinician in molecular diagnostics, genetic counselling and therapeutic choices. Several lines of evidence suggest the existence of common polymorphic variants of genes that modify the susceptibility to heart failure (modifier genes) (Mestroni et al., 2010).

The European Society of Cardiology (ESC) Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008 have been published by the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008. These guidelines have been developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM) (Task Force for Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of European Society of Cardiology, Dickstein et al., 2008).

This brief meeting report highlights the key findings of the Heart Failure 2010 Congress held in Berlin, Germany from 29 May to 1 June 2010, for which the editor of Annals of AlQuds Medicine, Dr. Haitham Idriss, was press registrant.

Websites:
http://www.annalqudsmed.com ,
http://www.escardio.org/congresses/hf2010/scientific/pages/scientific-programme.aspx
and:
http://spo.escardio.org/Welcome.aspx?eevtid=38

Implanted pulmonary pressure monitoring devices reduce heart failure hospitalisation

Implanting heart failure patients with a new device to monitor pulmonary artery pressure, involving wireless sensing communications technology, resulted in a 30 % reduction in heart failure hospitalisations at six months and a 38 % reduction in annualized (taking into account the entire follow up period averaging 15 months, calculated as an annual rate of decrease) in heart failure hospitalisations. The study reported by the phase III CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients (CHAMPION) Trial at the Heart Failure Congress 2010 showed reductions in pulmonary arterial pressures for patients implanted with the monitoring device, increases in the number of days alive and outside hospital and improvements in quality of life. This device has already been evaluated in a recent study for ambulatory assessment of pulmonary artery pressure in heart failure (Verdejo et al., 2007). "Identifying early rises in pulmonary arterial pressure is important because it's the most direct sign of congestion," said William Abraham, one of the co-principal investigators of the study from the Division of Cardiovascular Medicine at The Ohio State University Medical Centre (Columbus, Ohio). He added that until now the only available approach was for patients to monitor weight gain, which has a low sensitivity in predicting heart failure hospitalisations of only 10 to 20 %. "The idea is that if we identify elevated pressures we can quickly treat patients proactively, titrating their medications to bring them back into the normal range, thereby avoiding episodes of heart failure decompensation where patients often need emergency room admissions." Results of the trial are currently being used for regulatory approval of the CardioMEMS device around the world.

Genetically Targeted Therapy Shows Promise in Severe Heart Failure

The heart's ability to contract, and thus to pump blood and maintain oxygenation of the body, is determined by a continual re-loading of the sarcoplasmic

reticulum with calcium ions. SERCA2a is membrane bound enzyme expressed in the myocardium (Inesi et al., 2008). It is a P-type ATPase pump that regulates myocardial calcium cycling and contractility. SERCA pumps have been linked to a variety of human diseases (Hovnanian, 2007). Recent studies have established clear associations between depleted SERCA2a enzymes in cardiac cells and progression of end stage heart failure. "As the heart begins to fail the SERCA2a levels get depressed, leading to a vicious cycle where the heart fails even more," explained Dr. Greenberg, one of the authors of the study. MYDICAR® is a genetically targeted enzyme replacement therapy designed to restore levels of SERCA2a in the heart. With MYDICAR®, developed by CelladonCorporation (La Jolla, California), the SERCA2a gene is delivered using recombinant adeno-associated viral vector (AAV), a naturally occurring virus that approximately 90% of the population have been exposed to with no evidence of harm. MYDICAR® is provided in a single dose delivered directly into the coronary arteries during a short outpatient procedure, performed in a standard cardiac catheterization laboratory via a small incision in the upper leg. MYDICAR® is then carried to the heart muscle where it is taken up within the cells of the heart. Previous studies using reagents similar to MYDICAR® have shown delivery of the SERCA2a gene to skeletal muscle in humans results in persistence of gene activity for longer than four years. This study highlighted that the risk for clinical cardiovascular (CV) events was reduced by 50% for patients with severe heart failure receiving MYDICAR® as opposed to placebo. It is important to point out that this was a very small and early phase trial and further clinical research is required to support these promising preliminary findings.

Correction of iron deficiency with intravenous iron therapy improves renal function in heart failure

Impaired renal function affects many patients with chronic heart failure (Besarab et al., 2009; Silverberg et al., 2008; Silverberg et al., 2010). The inflammation related to heart failure impairs the release of iron from stores in the liver and macrophages. Patients with heart failure (HF) often have renal dysfunction and patients with kidney disease develop congestive HF, therefore the concept of cardio-renal syndromes evolved which can be a chronic or acute cardio-renal syndrome. This is known as chronic cardio-renal syndrome (Attanasio et al., 2010). Recent work from the nephrology literature suggests that addressing this iron deficiency by intravenous iron may improve renal function in patients with chronic renal disease (Silverberg et al., 2009). "Many patients with chronic heart failure have renal dysfunction which is strongly related to poor health outcomes. None of the therapies currently recommended for CHF patients have a favourable effect on renal function. Thus, there is great interest in treatments which may have renal protective properties," explained Professor Piotr Ponikowski, from the Medical University, 4th Military Hospital (Wroclaw Poland). A phase III study originally reported in 2009 has demonstrated that treatment with intravenous FCM (Ferinject®) in iron deficient chronic heart failure patients was well tolerated and significantly improved symptoms, NHYA functional class, six-minute-walk distances and quality of life. The treatment effect on renal function of Ferinject® was independent of the level of renal function at the start of the study, or of age, sex, CHF severity, magnitude of left ventricle dysfunction, the presence of anaemia and diabetes mellitus. The investigators were able to demonstrate that therapy with FCM in iron deficient

patients was associated with an improvement in renal function, already seen after 4 weeks, which persisted until the end of the study (6 months later).

New treatment strategy for heart failure patients with central sleep apnea

Central sleep apnea (CSA) occurs when the brain fails to send the correct signals to the diaphragm, causing patients to lose the natural pattern of breathing during sleep. CSA is an increasing problem in adults and children throughout the world. Breathing patterns in patients with CSA are characterized by cycles of increased breathing followed by shallow breaths with periods of no respiratory effort. It is different from obstructive sleep apnea (OSA), which occurs when lungs work normally but the breathing passages collapse temporarily during sleep. Sleep disruption has been linked with heart failure (Naughton and Lorenzi-Filho, 2009). Studies show that approximately 75% of Heart Failure patients have sleep disordered breathing, with half having CSA and half OSA (Sharma et al., 2010; Javaheri, 2010).

According to a Polish and US feasibility study presented at the Heart Failure Congress stimulation of the phrenic nerve has the potential to effectively treat central sleep apnea (CSA). In the current study, investigators from five centres in the US and Poland set out to explore whether stimulating the phrenic nerve (the nerve controlling the diaphragm) would prevent CSA. Clinical data showed phrenic nerve stimulation in patients with CSA and heart failure delivered improvements in the central apnea index, oxygen saturation levels and arousal index. "Heart failure patients, even those who appear to be doing well, hyperventilate probably as a result of subtle increases in their pulmonary artery pressure. Hyperventilation reduces CO_2 concentrations in the blood and brain, and as CO_2 levels fall below the apnea threshold the brain tells the body to stop breathing until CO_2 levels rise above that threshold again, " explained Professor William Abraham, one of the collaborating investigators from The Ohio State University (Columbus, OHIO).***Alpha-defensins: novel biomarkers in heart failure?***

A biomarker is a biochemical entity used to measure the progress of a disease or the effects of treatment on clinical outcome. In medicine the term refers to a protein measured in blood, whose concentration reflects the presence or severity of a disease state. Biomarker discovery, qualification and validation have traditionally been the domain of human clinical medicine and the preclinical research that underpins the drug discovery process.

Alpha-defensins are part of the innate immune system, and are present in the circulation during infection and non-infectious inflammation (Schneider et al., 2005; Soehnlein et al., 2009). These proteins are also involved in the lipoprotein metabolism in the vessel wall, favouring LDL and lipoprotein accumulation and modification in the endothelium and the extra cellular matrix. Low-grade inflammation might be an underlying mechanism during development and progression of chronic heart failure. Christensen and colleagues from Copenhagen University Hospital evaluated the plasma levels of alpha-defensins in 193 chronic heart failure patients and 98 healthy controls. The patients were followed up for a median of 2.6 years (range 0.5 to 3.9 years) with regard to mortality and new ischemic events. Their results suggest that alpha-defensin levels in chronic heart failure patients are associated with increased all-cause mortality and risk of new ischemic

events. Their study suggests that alpha-defensins may become useful cardiac biomarkers in cardiovascular research.

Research on disease pathogenesis and novel therapies for heart failure is urgently needed. New information about the pharmacogenomics of heart failure could be used to personalize and optimize heart failure therapy based on the patient's genetic profile. This is not merely science fiction; advances in post-genomic technologies will continue to propel personalized medicine from the bench to the bedside. Physicians (cardiologists in particular) will need to reshape clinical diagnostics paradigms, learn how to use new genomic information to change management decisions, and provide the patients with appropriate education and management recommendations (Mestroni et al., 2010).

Relevant Future Meetings

The Heart Failure Association will be having a winter meeting in 2011. The meeting will be held from 26 Jan 2011 - 29 Jan 2011 in Les Diablerets, Switzerland. This meeting will focus on integrative basic sciences relevant to heart failure. Further information may be found on their website: http://www.escardio.org/communities/HFA/meetings/Pages/winter-research-meeting.aspx.

The Kaufman Center for Heart Failure at the Cleveland Clinic and the American Association for Thoracic Surgery (AATS) have organised an educational event for health care providers specialising in the treatment of heart failure. The event entitled: '21st Century Treatment of Heart Failure: Synchronizing Surgical and Medical Therapies for Better Outcomes' will take place from 21-22 October 2010 at the InterContinental Hotel and Bank of America Conference Centre in Cleveland, Ohio. The meeting bring together two of America's leading cardiovascular specialty organizations to address the growing problem of heart failure. Therapies for heart failure are continuously evolving. Consequently there is an acute need to bring the leading experts together in educational events to share the latest reports and clinical trials on the current medical and surgical therapies for heart failure patients. Highlighting the key areas of activity in this area of research will increase the quality of care and the outcomes of therapy in heart failure patients.

Topics will include:

- Insights into Controversial Medical and Surgical Treatments
- Strategies for Slowing Heart Failure Progression with the Use of CRT-D
- Quality Metrics and their Impact on Cardiovascular Disease Practice
- Management of Acute Myocardial Infarction and Shock
- Surgical Management of Ischemic Cardiomyopathy
- Cardio-Renal Interactions
- Patient Selection for Mechanical Circulatory Support
- Long Term Management of the Patient on Mechanical Circulatory Support
- Contemporary Experience with New Pumps

Website: http://www.clevelandclinicmeded.com/live/courses/2010/heartfailure10/overview.htm

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