IRB protocol

A. Study Purpose and Rationale

Diastolic dysfunction has quickly been recongized as a serious condition, comparable in mortality rates to those of systolic dysfunction. Diagnostic tools have been limited. Previously, the widely accepted gold standard was the assessment of filling patterns as observed using standard Doppler. Standard Doppler assessed early and late filling velocities across the mitral valve as indices of diastolic function. Changes in E/A ratios have been widely accepted as diagnostic of diastolic dysfunction.

However LV relaxation and compliance are not the only determinants of early filling velocity. Early filling is also dependent upon LA pressure. LA pressure is determined by preload, ie volume, thus early filling velocity as measured by standard Doppler is subject to fluctuations in intravascular volume. Many studies have demonstrated the preload dependence of standard Doppler in its determination of E/A ratio. Thus, standard Doppler has been very limited in its diagnostic validity of diastolic dysfunction in patients in states of volume flux. HD patients for example are volume overloaded at times and at times hypovolemic, and have expected large fluctuations in their E/A ratios on Doppler. This poses a diagnostic challenge for the clinician assessing ESRD HD patients for diastolic dysfunction. This can be extrapolated to other patient populations such as those with co-existing systolic heart failure during times of chf exacerbations.

TDI has made advancements in the field of imaging and has emerged as a preload independent diagnostic tool for assessment of diastolic function. Some studies have questioned this, however most do not deny that it is far superior to standard echo. CMR has been established as a more advanced tool for assessing many aspects of cardiac physiology and pathology including advancements being made in CMR's diagnostic abilities with respect to diastolic dysfunction.

Studies have established CMR as a valid tool in assessing diastolic dysfunction and determining diastolic dysfunction severity. CMR has many advantages over standard Doppler.

However, CMR has not yet been scrutinized for its accuracy in diagnosing diastolic dysfunction in the setting of volume fluctuations. We are proposing a study of the effect of preload fluctuation on the diagnostic indices of diastolic function in patients with ESRD pre and post HD.

B. Study Design and Statistical Analysis

Study Design
Subjects will be recruited from the outpatient HD clinic at CUMC.

Statistical analysis:
Significance in the difference between the pre and post HD measurements will be assessed using a paired t-test.

Power analysis
The number of subjects enrolled

C. Study Procedure

Subjects will undergo standard HD sessions without interruption or variation during the session. Subjects will have a CMR performed prior to the session. Subjects will have a CMR performed at 1 hour after completion of HD. Each CMR will take a max of 90mins. Each subject will participate in a pre-assessment that will include a medical history, social and family history, vital signs (as are taken standard prior to and post HD), weight, blood urea level. Subjects will not experience any pain during the CMR.

The involvement of each subject will only included the day of the CMR, no further testing will be required at this stage.

The duration of the entire study will be < 3 months.

CMR:

"CMR exams were performed using 1.5 Tesla scanners (General Electric). Cine-CMR used a commercially available 2D steady state free precession pulse sequence. Images were acquired in contiguous short axis slices from the level of the mitral valve annulus through the LV apex. Typical parameters were as follows: repetition time (TR) 3.5 msec, echo time (TE) 1.6 msec, flip angle 60°, in-plane spatial resolution 1.9 mm x 1.4 mm, slice thickness 6mm, inter-slice gap 4mm. In accordance with the clinical trial protocol, delayed enhancement CMR (DE-CMR) was performed for assessment of LV infarct size."'

"Automated CMR Segmentation

LV Systolic Function and Morphology

LV volumetric and myocardial mass quantification was performed automatically using LV-METRIC. For assessment of chamber volumes, the algorithm automatically segments the

endocardial border excluding papillary muscles and trabeculae from the blood volume.[8] Epicardial segmentation was also performed for automated volumetric quantification of LV mass.[14] LV-METRIC user input included identification of the slice range to be segmented and definition of the valve annulus. Optional corrections were provided by manually contouring to restrict region-growth and adjusting blood sensitivity.

End-diastolic volume (EDV) and end systolic chamber volume (ESV) were calculated using Simpson's method, with EF calculated as [EDV-ESV]/EDV*100. Automated border detection of end-diastolic endocardial and epicardial contours were used to quantify LV mass,[14] which was calculated as the product of myocardial volume and specific gravity ([EpiEDV-EDV]*1.05). "

D. Study Drugs
N/A

E. Medical Device

F. Study Questionnaires
N/A

G. Study Subjects
Excluded : Subjects with arrhythmia, CAD,
Included: Adult subjects who have been on dialysis for at least 1month, TIW.

H. Recruitment of Subjects
Patients will be recruited from our out patient HD center.

I. Confidentiality of Study Data

J. Potential Conflict of Interest
N/A

K. Location of the Study
The study will be conducted at CUMC.

L. Potential Risks
The risks to the patients are minimal to none. No contrast material will be used. Patients with anxiety/averse emotional reactions/ Clostrophobia will be excluded from the study so no sedating medications will be administered.

M. Potential Benefits
Higher quality assessment of the patients cardiac function.

N. Alternative Therapies
N/A

O. Compensation to Subjects
N/A

P. Costs to Subjects
There will be no cost to subjects.

Q. Minors as Research Subjects
No minors will be involved in this project.

R. Radiation or Radioactive Substances
N/A