31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Human Feasibility study of Hemodynamic Monitoring via Continuous Intrathoracic Impedance monitoring

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Abstract— **The ultimate hemodynamic sensor for an implantable device would provide information about cardiovascular performance including systolic function, diastolic function, preload, and afterload. We examined the potential clinical utility of simultaneous measurement of left ventricular pressure and continuous intrathoracic impedance in a group of 20 patients undergoing acute intravenous ablation for atrial fibrillation. Following baseline measurements of traditional left ventricular (LV) conductance volume (control), LV pressure and conductance measurement were repeated using alternate impedance stimulation and sensing vectors that encompassed combinations of the lung, left ventricle, right ventricle and left atrium, respectively. Various relative indices of LV function, including end systolic pressure to volume (conductance) ratio, end diastolic pressure to volume (conductance) ratio, and preload recruitable stroke work (analog) were derived by combining real-time pressure and conductance. The raw morphometry of the LV vector seemed to most closely resemble the gold standard LV conductance volume. For this vector, strong linear correlations between LV pressure and end systolic conductance (r=0.84±0.14), end diastolic conductance (r=0.78±0.10) and preload recruitable stroke work analog (r=0.93±0.05) were observed. The LV vector provides a robust continuous intracardiac hemodynamic signal that may be useful for quantifying cardiovascular function.**

I. INTRODUCTION

The ultimate hemodynamic sensor for an implantable device would provide information about multiple aspects of cardiovascular performance including systolic function (the ability of the ventricle to generate pressure), diastolic function (the ability of the ventricle to fill), preload (the extent of ventricular filling), and afterload (the forces opposing ejection). To this end, pressure-volume plane analysis is a well known research tool to help quantify overall cardiovascular function [1],[2],[3].

Besides providing potentially life saving therapies, some implantable devices including pacemakers, ICD's and CRT-D devices also contain detailed diagnostic information about the patient including long term trends of heart rate, heart rate variability, respiration trends, patient activity and atrial and ventricular tachyarrhythmia recurrence. Some experimental devices currently under investigation also measure intracardiac chamber pressure [4],[5]. Intermittent monitoring of pulmonary fluid accumulation via intrathoracic impedance monitoring has also been shown to be a clinically useful diagnostic tool that can identify patients at significant risk for worsening heart failure events with reasonable accuracy [6],[7],[8]. However, it is possible that the clinical utility of intrathoracic impedance monitoring could be extended by performing continuous impedance measurements within a chamber of interest such as the left ventricle. Furthermore, the combination of a device based impedance measurement with a device based pressure measurement could result in a clinical tool to analyze cardiovascular function in a manner similar to the pressure-volume plane. We examined the potential clinical utility of simultaneous measurement of left ventricular pressure and continuous intrathoracic impedance from a variety of electrode positions in a group of patients undergoing intravenous ablation for atrial fibrillation. .

II. METHODS

The Advanced Vector Impedance Cardiography System to Estimate Left Ventricular Function (ADVISE-LVF) clinical trial was a prospective single center feasibility trial that enrolled 20 subjects. The trial was approved by the internal review board and all patients provided written informed consent. Adult subjects referred for catheter ablation (isolation) of the pulmonary veins for the treatment of symptomatic atrial tachyarrhythmias were included. Subjects with a history of aortic valve disease or aortic aneurysm were excluded. Patients were typically anesthetized with a combination of narcotic and intravenous or volatile anesthetic.

"Gold standard" LV pressure and conductance volume measurements were obtained using a 12 electrode combination pressure-conductance volume catheter (Model #CA-72103-PNA, CD Leycom, Zoetermeer, The Netherlands) that was advanced into the apex of the LV via femoral arterial access using fluoroscopic guidance. The pressure volume catheter was coupled to a signal recorder-processor (CF 512, CD Leycom). This device allowed simultaneous real time recording of the cardiac impedance signal. Standard multi electrode electrophysiology catheters were used for all alternate vector impedance measurements. Catheters were positioned in the right ventricular apex, distal coronary sinus, right atrial septum (medial christa terminalis) or proximal subclavian vein via standard venous access. A balloon catheter (model# PTS404, NuMed, Hopkinton NY) was advanced to the IVC via standard

Manuscript received April 7, 2009. This work was supported by Medtronic, Inc. Minneapolis, MN.

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978-1-4244-3296-7/09/$25.00 ©2009 IEEE

venous access in order to allow repetitive transient reductions in LV preload by brief (2-5s) inflation of the balloon.

LV pressure measurements were performed continuously throughout the impedance measurement interventions. Control impedance measurements were obtained at baseline using conductance catheter techniques. Since the goal of this study was not to determine actual LV volume, the conductance volume catheter signal was not calibrated into units of actual volume, but was used as a relative comparison of the morphometry of true LV volume. Hence, all global conductance volume measurements were converted to units of electrical conductance.

Following baseline measurements of traditional LV conductance volume, LV pressure and conductance measurement were repeated using alternate impedance stimulation and sensing vectors. Randomized impedance measurements were performed using the current driving vectors described in table 1 and figure 1.

Various relative indices of LV function, including end systolic pressure to volume (conductance) ratio (ESPVR), end diastolic pressure to volume (conductance) ratio, and preload recruitable stroke work (PRSW), were derived using commercial (Conduct NT, CD Leycom) or custom IDL software by combining real-time pressure and conductance.

TABLE I
MEASURED ELECTRODE VECTOR COMBINATIONS

Combination	Driving Electrodes		Sensing Electrodes	
OptiVol	RV	SC	RV	RV
Lung	RV	SC	CS	RV
LV	RV	CS	RV	RV
Tricuspid	RV	RA	RV	RV
Atrial	CS	RA	CS	CS

RV=right ventricle, RA=right atrium, CS=Coronary sinus, SC= subclavian

III. RESULTS

A total of 20 subjects were enrolled between February and November 2007. One subject failed to complete the protocol due to technical equipment malfunction. Demographic data on the remaining 19 subjects are shown in table 2. Acceptable IVC occlusion data was acquired in 5 subjects. The average duration of the data collection procedure was 23±7min (range: 16-40 min). No significant changes in any hemodynamic parameter were observed throughout the study procedure. Amplitude and changes in raw impedance measurements from the various conductance vectors are shown in table 3. Measurement of impedance was attempted, but not completed, from all vectors in all patients since the data collection system was not capable of recording impedances greater than 48 ohms.

Of the measured vectors, the "LV" vector morphology seemed most similar to the standard conductance catheter volume signal. Sample raw LV pressure, "conductance catheter" and LV-RV vector conductance are shown in figure 1. The morphometry of both signals is consistent with LV volume morphology including rapid filing, diastasis, atrial systole and LV contraction. The derivative of the conductance signal, an analog of mitral and aortic valve flow, shows features consistent with early filling ("e" wave) atrial contraction ("a" wave) and aortic flow patterns. Figure 2 shows representative pressure conductance loops from one subject with IVC occlusion for both the conductance catheter technique and for conductance measurements performed from the LV vector.

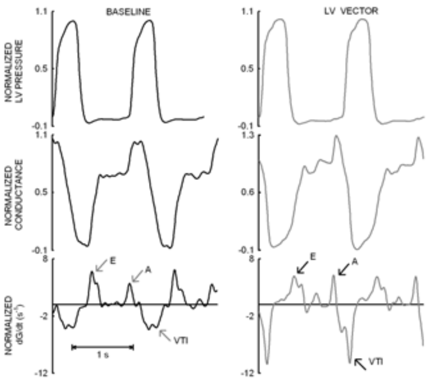

Fig. 1. Raw LV Pressure (top), conductance (center), and the derivative of conductance (dG/dt;bottom) using gold standard conductance catheter techniques (left) and pacemaker LV lead configuration (right): Distinct "E" and "A" waves are observable in the derivative of both conductance signals. The negative portion of the dG/dt signal is likewise analogous to ejection velocity, similar to aortic velocity time integral (VTI) measurements.

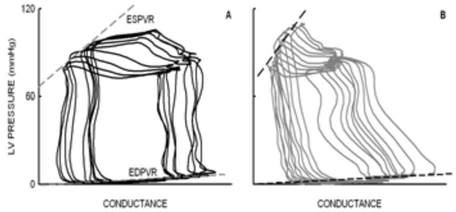

Fig. 2. Raw pressure-conductance (volume) loops during transient IVC occlusion in one subject using gold standard conductance catheter (A) and LV- vector (B): Dashed lines represent calculated ESPVR and EDPVR, respectively.

Figures 3-5 show the sample calculation of the ESPVR , EDPVR and PRSWA for this subject. Table 4 shows the average linear correlation coefficients for all 5 patients wit IVC occlusions. The high linear correlation values calculated indicates that it is feasible to calculate indices of cardiovascular function using conductance data derived from the LV lead.

IV. DISCUSSION

A. General

The main finding of this pilot human study is that it is feasible to obtain an intracardiac conductance signal generally proportionate to LV volume using conventional CRT device lead configurations. Alone, such a signal could be used to derive several important indices of LV systolic and diastolic function as well as LV preload. Furthermore, if combined with an analogue of LV pressure, quantification of all four components cardiovascular function including systolic function, diastolic function, preload, and afterload may also be feasible.

TABLE II
SUBJECT DEMOGRAPHICS (N=19)

Age	55±12 yr
Male	16(84%)
Ejection Fraction	57±6%
Congestive Heart Failure	1(5%)
Hypertension	6(32%)
Coronary Artery Disease	4(21%)
Antiarrhythmics	6(32%)
Anticoagulation	10(53%)
Beta-blockers	5(26%)
Diuretics	4(21%)
Antihypertensives	4(21%)

*n=15

The pressure volume plane has long been considered the scientific gold standard for evaluating cardiovascular function. This is due in part to the fact that PV plane analysis considers the major mechanical determinants of myocardial performance, including both mechanical stress and strain. LV pressure and volume are related through myocardial elastance. Thus, the pressure volume plane enables quantification of changes in myocardial elastance throughout the cardiac cycle.

Lone pressure measurements provide primarily an index of mechanical stress, or the force acting on the tissue. Likewise, flourscopically or echocardiographically derived indices of dimension such as ventricular diameter, end diastolic volume, ejection fraction, and dyssynchrony are primarily indices of strain, or the mechanical deformation of tissue in response to the applied stress. Thus, pure echocardiographic based indices of chamber strain do not consider the associated stress or pressure that led to the resultant strain. However, by combining stress and strain into a single evaluation tool, PV plane analysis is able to objectively quantify all 4 major components of cardiovascular function including preload, afterload, systolic, and diastolic function, independent of loading conditions.

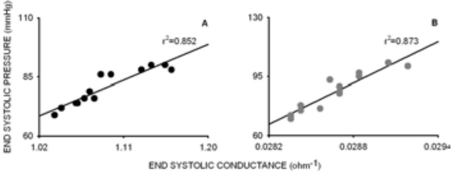

Fig. 3. ESPVR calculation for one representative subject using gold standard conductance catheter (A) and LV- vector (B).

Systolic function describes the ability of the ventricles to eject blood into the afterload or arterial system. On a cellular level, it describes the ability of the myocyte to develop force against a given afterload for any given initial stretch or preload. Many common clinical indices of cardiac performance such as cardiac index (or output), stroke volume, aortic velocity time integrals, ejection fraction, stroke work and dP/dt are all load dependent. This implies that a change in any of these indices may be due simply to changes in preload or afterload, and not necessarily to changes in actual systolic function. Therefore, ventricular systolic function is best described using load independent indices such as the end systolic pressure volume curve (ESPVR) or preload recruitable stroke work (PRSW).

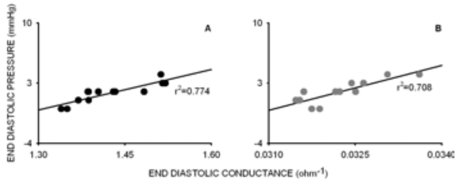

Fig. 4. EDPVR calculation for one representative subject using gold standard conductance catheter (A) and LV- vector (B).

Likewise, "Diastolic function" is the ability of the left ventricle to fill. The 4 key phases of diastole include active relaxation of the ventricle, passive or early filling, diastasis or reduced filling, and active filling resulting from atrial contraction. The rate and extent of active relaxation can be indicated by either the time constant of isovolumic relaxation (tau) or by peak negative LV dP/dt. The later phases of LV chamber filling are completely described by the EDPVR or passive ventricular stiffness. Delayed or incomplete relaxation, myocardial hypertrophy, or other disease states lead to pathologic stiffening of the LV that limits filling and, hence, overall cardiovascular performance. Indeed, the recognized clinical experts in diastolic function have identified the LV EDPVR as the quintessential index of identifying diastolic heart failure [2]. The present results show that it is feasible to obtain an analogue of LV volume that, if combined with LV pressure, would perhaps reveal proportionate changes of the EDPVR.

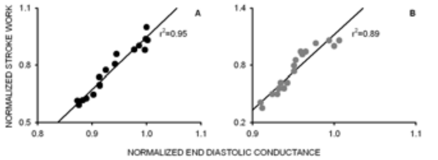

Fig. 5. PRSW calculation for one representative subject using gold standard conductance catheter (A) and LV- vector (B).

Preload is defined on a cellular scale as the length of the myocyte at the time of contraction. On a ventricular scale it is defined as LV end diastolic volume. Preload is perhaps the most important parameter for monitoring CHF patients. Since the LV vector conductance provides an analogue of LV volume as demonstrated by figures 1 and 2, the maximum conductance could provide a clinically useful analogue of the gold standard of preload measurement.

Afterload is defined as the forces opposing ejection. It is primarily determined by the mechanical resistance and compliance of the arterial system. Other determinants of afterload include the mechanical status of the aortic outflow tract and the aortic valve. Arterial pulse wave reflection can also influence LV afterload. A useful index of afterload would be a key parameter to monitor arterial hypertension. LV or arterial systolic pressure and left ventricular wall stress are indices of LV afterload. However, these primarily reflect arterial vascular tone and not necessarily compliance or wave reflection. Effective arterial elastance (EA) is an index of LV afterload that considers both resistance and compliance of the arterial vasculature. EA is defined as the ratio of LV end systolic pressure to stroke volume. Since the LV vector seems to correspond to LV volume, the combination of LV pressure and LV conductance could provide a useful analog of afterload and hypertension.

TABLE III
SUMMARY IMPEDANCE DATA (N=19)

	Impedance (ohm)			
Vector	**Mean**	**Min**	**Max**	**Δ**
Control	1.0±0.3	0.9±0.3	1.2±0.4	0.3±0.2
OptiVol	39.0±7.0	38.3±7.0	40.2±7.5	2.0±1.0
Lung	35.3±6.2	34.8±6.2	35.8±6.2	1.0±0.4
LV	30.5±6.9	28.8±6.4	32.7±7.4	3.9±1.5
Tricuspid	27.3±6.4	25.8±6.6	29.1±6.7	3.3±1.6
Atrial	27.4±5.4	26.0±5.4	29.0±5.7	3.0.±0.9

The present analysis has focused primarily on the LV impedance vector, since this vector seemed to most closely approximate LV chamber volume. However, we also recorded data for multiple other vectors. Besides the LV vector, the "Tricuspid" vector also gave raw conductance and pressure conductance loops that often closely resembled traditional LV pressure conductance volume loops. However, this conductance is likely proportionate to RV, rather than LV dimension or volume. The "Atrial" vector morphometry generally seemed to behave more like an atrial volume signal, with some apparently superimposed ventricular morphometry (data not shown). The lung vector had varying morphometry, occasionally resembling LV or atrial morphometry, respectively. However, the results of the present trial indicate that for the purpose of monitoring cardiovascular function, the LV vector appears to be superior.

TABLE IV
CORRELATION COEFFICIENTS (R) FOR ESPVR, PRSWA AND EDPVR

	r		
	Conductance Catheter Vector	LV Vector	p
ESPVR	0.95±0.02	0.84±0.14	0.18
PRSWA	0.88±0.07	0.93±0.05	0.26
EDPVR	0.77±0.10	0.78±0.10	0.87

Mean±SD

B. Limitations

Standard temporary electrophysiology catheters were used in place of permanent catheters. A temporary catheter in the subclavian vein was also used to approximate the device can. Also, it was not possible to simultaneously record both conductance catheter and alternate vector impedance measurements due to hardware limitations. Therefore, these data were recorded in a serial fashion. However, we observed no significant changes in basic hemodynamic parameters including heart rate, LV pressure or dP/dt throughout the study period.

V. CONCLUSIONS

The LV vector provides a robust continuous intracardiac hemodynamic signal that may be useful for quantifying cardiovascular function in both animal and human subjects. Such a signal could be used to derive several important indices of LV systolic and diastolic function as well as LV preload.

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