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ORIGINAL ARTICLE

Use of Pressure-volume Conductance Catheters in Real-time Cardiovascular Experimentation

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Background Most applications of pressure-volume conductance catheter measurements assess cardiovascular function at a single point in time after genetic, pharmacologic, infectious, nutritional, or toxicologic manipulation. Use of these catheters as a continuous monitor, however, is fraught with complexities and limitations.

Methods Examples of the limitations and optimal use of conductance catheters as a continuous, real-time monitor of cardiovascular function are demonstrated during inotropic drug infusion in anesthetised rats.

Results Inotropic drug infusion may alter ventricular dimensions causing relative movement of a well-positioned catheter, generating artifacts, including an abrupt pressure rise at end-systole that leads to over estimation of indices of contractility (max dP/dt) and loss of stroke volume signal. Simple rotation of the catheter, echocardiography-guided placement to the centre of the ventricle, or ventricular expansion through crystalloid infusion may correct for these artifacts. Fluid administration, however, alters left ventricular end-diastolic pressure and volume and therefore stroke volume, thereby obscuring continuous real-time haemodynamic measurements.

Conclusions Pressure-volume artifacts during inotropic infusion are caused by physical contact of the catheter with endocardium. Repeated correction of catheter position may be required to use pressure volume catheters as a continuous real-time monitor during manipulations that alter ventricular dimensions, such as inotropic therapy.

Keywords Pressure-volume conductance catheter • Pressure volume loop • Dobutamine infusion • Max dP/dt • End-systolic pressure volume relationship

Introduction

Measurement of left ventricular pressure and volume is a valuable means for characterising cardiac function [1–3]. From these measurements and their derivatives, parameters of left ventricle (LV) function and energetics such as stroke volume (SV), stroke work (SW), ejection fraction, pre-load recruitable stroke work, arterial elastance, end-systolic pressure-volume relationship (ESPVR), maximum dP/dt, minimum dP/dt, and relaxation time constants can be obtained. In 1984, Baan and colleagues designed a conductance catheter that could acquire simultaneous pressure-volume (PV) measurements continuously in large animals [4]. This catheter eliminated the need for careful synchronisation of left

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ventricular manometric pressure readings with volume measurements from labour intensive, costly imaging methods like echocardiography, sonomicrometry, or MRI. A miniature PV catheter for mice was introduced in 1998 [5] and has been used to elucidate the haemodynamic implications of many rodent models of cardiovascular disease [6–9].

The PV catheter passes a high-frequency low-amplitude current through two sets of electrodes that are ideally oriented along the longitudinal axis of the LV and simultaneously measures electrical potentials that are proportional to ventricular volume. With calibration, these signals can be converted to instantaneous LV blood volume measurements. Also integrated into the catheter is a pressure transducer allowing real time pressure-volume loop generation. While the PV catheter is easier to use and more direct than many cardiac imaging techniques, optimal position and orientation of the catheter in the ventricle at various haemodynamic states must be maintained for accurate measurements. Pacher and colleagues described a comprehensive guide for using this technology [1,3]. They recommended that the PV catheter be adjusted and optimised prior to recording data, ensuring capture of the maximum LV blood volume signals.

Many applications of PV catheters assess cardiovascular function at a single point in time after genetic, pharmacologic, toxicologic, infectious, environmental or nutritional manipulation of an animal, and these data are compared to control animals without such interventions. These applications require delineation of steady state conditions before and after treatment or intervention, but neglect the time course of the transition. PV conductance catheters can be used as a continuous real-time monitor of cardiovascular function but such use is more complicated and somewhat more limited than at specific points in time. Continuous experiments are often pharmacologic interventions that produce acute haemodynamic changes, on the order of minutes to hours, and can be performed while the PV catheter remains in situ for the duration of the treatment [10,11]. We have found that such real-time monitoring during pharmacologic treatment can only be performed with frequent manipulation to optimise position, which can lead to disruptions in continuous signals. Some have presented real-time data from PV catheters [12,13], but make no mention of the need for periodic catheter placement optimisation.

We demonstrate the limitations of continuous pressure and volume monitoring with PV catheters and methods to overcome them in a model of inotropic drug infusion, dobutamine. This beta adrenergic agonist increases SV and cardiac output through a beta-1 adrenergic mediated positive inotropic response on myocardium and beta-2 adrenergic mediated peripheral arterial and venous dilatation [14]. Dobutamine, therefore, increases contractility while, at the same time, decreases preload and afterload, a combination of effects that tends to decrease the volume of the ventricle. This drug also has the pharmacokinetic advantage of a short serum half-life of three minutes so that haemodynamics changes reach steady-state within 10 minutes of starting an infusion. Real-time continuous catheter measurements can accurately capture swift changes in the pharmacodynamic profile of dobutamine infusion. Our study suggests measures to be taken for optimal use of this technique as a real-time monitor. Researchers performing experimental interventions eliciting similar dynamic cardiovascular responses can benefit from this method of catheter use.

Research design and methods

Rodent Preparation and Catheterisation

All procedures were approved by the Institutional Animal Care and Use Committee at Steward St. Elizabeth's Medical Center. Male Sprague-Dawley rats (400-450 grams; Charles River Laboratories, Wilmington, MA) were anaesthetised with pentobarbital (50 mg/kg, intraperitoneal, i.p.), weighed, and an intraperitoneal catheter was placed for continuous infusion of pentobarbital (30 mg/kg/hr). The neck, chest and inguinal areas were shaved and the animal placed supine on a heating pad (#TP-500; Gaymar Industries, Orchard Park, NY) set to maintain rectal temperatures between 36.7-37.0^{0}C. A tracheotomy was performed with a 14-gauge cannula secured and connected to a custom ventilator system which delivered 153 mL/min O_2 through a solenoid valve controlled by a computer (Labview Express 7.0; National Instruments, Austin, TX) at a respiratory rate of 96 breaths per minute, an I:E ratio of 1:3, and an approximate tidal volume of 1.6 mL.

The right femoral artery and internal jugular vein were exposed and cannulated with polyethylene-50 (PE-50) tubing. Both cannulas were de-aired with heparinised saline (2 U/mL) and joined together by a single stopcock connected to a pressure transducer (#TRN050; Kent Scientific, Torrington, CT). Toggling the stopcock allowed acquisition of either the arterial or central venous pressures. A pressure-volume conductance catheter (#SPR-869; Millar Instruments, Houston, TX) was inserted via an arteriotomy in the right carotid artery and advanced retrograde across the aortic valve and into the left ventricle. The right femoral vein was cannulated with PE-50 tubing, and albumin (#A7906, 10% in normal saline; Sigma–Aldrich, St. Louis, MO) delivered through it at 0.25 mL increments until left ventricular PV loops showed the four distinct phases of the cardiac cycle. The sternum was removed through bilateral, anterolateral, vertical thoracotomies and a loop of suture was wrapped around the inferior vena cava (IVC). Preload on the heart was transiently decreased by pulling up on the suture over 7-10 heart beats to obstruct IVC blood flow.

Data Acquisition

Arterial and venous pressures were transduced to a signal amplifier (#TRN005; Kent Scientific, Torrington, CT), digitised (PowerLab/8SP; ADInstruments, Colorado Springs, CO) and recorded in LabChart software (version 7.3.3; ADInstruments, Colorado Springs, CO). Signals from the pressure-volume conductance catheter (MPVS-300 system; Millar