Impact of left atrial appendage exclusion on left atrial function

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Objectives: We sought to investigate the short-term and midterm effects of left atrial appendage exclusion on left atrial function. Left atrial appendage exclusion is considered a possible therapeutic option for stroke prevention in patients with atrial fibrillation. Favorable outcomes have encouraged widespread use of left atrial appendage exclusion for cardiac surgical patients—even for patients in sinus rhythm who have stroke risk factors; however, the chronic effects on left atrial function of left atrial appendage exclusion are unclear.

Methods: Nineteen mongrel dogs (29.7 ± 5.2 kg) in sinus rhythm were studied. The Doppler signals from the pulmonary venous flow, transmitral flow, and tissue Doppler imaging of mitral annular motion were obtained before and after left atrial appendage exclusion. Dogs were evaluated in the same manner at 7 days (n = 2), 30 days (n = 7), or 90 days (n = 10) after left atrial appendage exclusion.

Results: Except for a significant increase in early diastolic transmitral flow velocity after left atrial appendage exclusion ($P = .01$), no significant differences were found in any parameters related to the transmitral flow and tissue Doppler imaging measurements throughout follow-up. The systolic components of pulmonary venous flow at follow-up revealed a significant reduction relative to baseline (peak systolic velocity $P < .0001$, systolic velocity-time integral $P < .0001$), despite the lack of significant changes in left atrial pressure, left ventricular volume, and stroke volume.

Conclusion: Left atrial appendage exclusion may affect left atrial reservoir function in the short-term and midterm periods. Further long-term studies with more clinically relevant models are needed.

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Atrial fibrillation (AF) is a major risk factor for stroke, a common cause of serious disability and death.[1,2] Congestive heart failure is often complicated by AF and promotes the development of AF even in patients with sinus rhythm.[3,4] The left atrial appendage (LAA) is a major source of atrial thrombi in patients with AF.[5,6] LAA exclusion has therefore been considered a potential therapeutic option for stroke prevention in patients with AF. Favorable outcomes of LAA exclusion in surgical patients have encouraged widespread use of this procedure, extending it to include patients in sinus rhythm who have stroke risk factors.[7] Although some in vitro[8] and in vivo[9-11] studies have reported that LAA exclusion can alter left atrial (LA) compliance, the chronic impact of LAA exclusion on LA and left ventricular (LV) functions still remain unclear.

Recently, pulsed Doppler analysis of pulmonary venous (PV) flow has provided additional information about atrial filling and function, which has been used in conjunction with the transmitral flow spectra or tissue Doppler imaging (TDI) of mitral annular motion to enhance assessments of abnormalities of ventricular

Abbreviations and Acronyms

AF = atrial fibrillation
CO = cardiac output
EDV = end-diastolic volume
EE = epicardial echocardiography
EF = ejection fraction
ESV = end-systolic volume
LA = left atrium
LAA = left atrial appendage
LAP = left atrial pressure
LV = left ventricle
PV = pulmonary vein
SV = stroke volume
TDI = tissue Doppler imaging
VTI = velocity-time integral

filling.[12-20] With the pulsed Doppler technique, the relationship between the PV flow pattern and dynamic changes of the LV and LA can be investigated under several different conditions in animals and human beings[12-15] and therefore used to assess the changes in LA or LV diastolic function resulting from LAA exclusion.

Materials and Methods

Nineteen mongrel dogs (29.7 ± 5.2 kg) in sinus rhythm were used in this study. This study was approved by the Cleveland Clinic's Institutional Animal Care and Use Committee, and all animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" (http://www.nap.edu/catalog/5140.html).

To evaluate the short-term and midterm effects of LAA exclusion on LA and LV functions in dogs, the LAA was excluded while the heart was beating with a novel exclusion device.[21] Hemodynamic and echocardiographic measurements were performed before and after LAA exclusion. Dogs were then evaluated at 7 days (n = 2), 30 days (n = 7), or 90 days (n = 10) after LAA exclusion in the same manner.

Study Protocol and Surgical Procedures

Initial study. All surgical procedures were performed under sterile conditions. The animals were anesthetized with intravenous thiopental (20 mg/kg) and ventilated through an endotracheal tube by a respirator (Servo Ventilator 900C; Siemens-Elema AB, Solna, Sweden). Anesthesia was maintained with isoflurane (0.5%-2.5%). The animals were placed in the right lateral position with electrocardiographic leads attached to the extremities. A left lateral neck incision was made to isolate the left carotid artery for arterial pressure monitoring.

A left thoracotomy was performed at the fourth intercostal space to obtain access to the heart. The pericardium was opened, and the heart was suspended in a pericardial cradle to expose the LAA. A 14-gauge angiocatheter was inserted into the left upper PV to monitor the LA pressure (LAP). With epicardial echocardiography (EE), 2-dimensional (2D) and all Doppler echocardiographic images were obtained. Hemodynamic data, including heart rate, systemic arterial pressure, and LAP, were also collected at baseline. Ventilatory support was transiently stopped during data-acquisition periods. Hemodynamic parameters were digitized in real time at a sampling rate of 200 Hz with a data-acquisition system (PowerLab; AD Instruments, Inc, Mountain View, Calif) and stored on a hard disk for subsequent analyses with a custom-made visual basic program on Excel software (Excel 2000; Microsoft Corporation, Redmond, Wash).

After all baseline data were obtained, the LAA was occluded with a simple device that permitted LAA exclusion from the outer surface of the heart while the heart was beating. Blood flow into the LAA was assessed before and after the LAA exclusion by 2D EE. If the device was not precisely placed at the base of the LAA, the device was simply repositioned and reapplied in the proper location[21,22] for successful exclusion of the LAA. After LAA exclusion, echocardiographic and hemodynamic studies were repeated in the same manner. The interval between the baseline data acquisition and postexclusion data acquisition was less than 10 minutes for all animals. After closure of the pericardium, the chest was closed with a chest drainage tube in place. Animals were followed up for 7 days (n = 2), 30 days (n = 7), or 90 days (n = 10). With the exception of analgesics and antibiotics, no additional medications were administered during the postoperative period.

Terminal study. On the day of the terminal study, animals were placed under general anesthesia according to the protocol of the initial study. A right inguinal incision was made to isolate the right femoral artery for continuous monitoring of arterial pressure. The chest was reopened from the original thoracotomy incision, and the pericardium was reopened to expose the LAA occlusion device. Hemodynamic assessment and EE were performed in the same manner as described for the initial study to evaluate the short-term and midterm effects of LAA exclusion on LA function.

Echocardiographic Measurements

Echocardiographic examinations were performed with a Sequoia 512 digital ultrasonographic system (Siemens, Mountain View, Calif) with a high-frequency transducer (frequency 5-7 MHz). All Doppler echocardiographic and TDI images were obtained and recorded during three to five consecutive cardiac cycles in sinus rhythm.

The LA body area was measured by planimetry in the apical 4-chamber view. The LA body volume was also assessed by a biplane area-length method from the apical 4- and 2-chamber views. It is true that the biplane long-axis method relies on various geometric assumptions. To assess the potential error introduced by our method in this animal series, we validated it against a criterion standard of 3-dimensional echocardiography[23,24] with real-time 3-dimensional data obtained by Vivid 7 echocardiographic machine and Tomtec software (Tomtec Gmbh, Unterschlessheim, Germany). Bland–Altman analysis[25] showed 95% limits of agreement of −2.4 and +7.4 mL, indicating that our method used for LA volume analyses in this animal series, although not perfect, was accurate enough to track changes in LA volumes. The LV end-diastolic volume (EDV) and end-systolic volume (ESV) were measured by single-plane Simpson rule. LV ejection fraction (EF) was calculated by the following equation: $100 \times (EDV - ESV)/EDV$. The LV stroke volume (SV) was calculated as the difference

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