Reservoir and conduit function of right atrium: impact on right ventricular filling and cardiac output

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The purpose of this study was to investigate the relationship between right atrial (RA) reservoir and conduit function and to determine how hemodynamic changes influence this relationship and its impact on cardiac output. In 11 open-chest sheep, RA reservoir and conduit function were quantified as RA inflow with the tricuspid valve closed versus open, respectively. Conduit function was separated into early (before A wave) and late (after A wave) components. The effects of inotropic stimulation, partial pulmonary artery occlusion, and pericardiomyopathy were tested. At baseline with the pericardium intact, reservoir function accounted for 0.56 (SD 0.13) of RA inflow, early conduit for 0.16 (SD 0.07), and late conduit (during RA contraction) for 0.16 (SD 0.07), and inotropic stimulation decreased conduit function and increased reservoir function, but these effects did not reach statistical significance. With partial pulmonary artery occlusion, early conduit function fell to 0.20 (SD 0.11) (P < 0.04), and the conduit-to-reservoir ratio decreased by 41% (P < 0.03). Similarly, after pericardiomyopathy, early conduit function fell to 0.14 (SD 0.09) (P < 0.004), reservoir function increased to 0.72 (SD 0.08) (P < 0.04), and, consequently, the early conduit-to-reservoir ratio decreased by 63% (P < 0.006). Cardiac output was inversely related to the conduit-to-reservoir ratio (r = 0.39, P < 0.001). This study demonstrated that the right atrium adjusts its ability to act more as a reservoir than a conduit in a dynamic manner. The RA conduit-to-reservoir ratio was directly related to the right ventricular pressure-RA pressure gradient at the time of maximum RA volume, with increased ventricular pressures favoring conduit function, but it was inversely related to cardiac output, with an increase in the reservoir contribution favoring improved cardiac output.

METHODS

Eleven adult sheep (25–30 kg) were anesthetized with ketamine hydrochloride (27 mg/kg im) and Pentothal Sodium (6.8 mg/kg iv) and then intubated and ventilated (Siemens, Munich, Germany) with supplemental inhalational isoflurane (1.5–3%). A median sternotomy was performed, leaving the pericardium intact. Ultrasonic flow probes (10- to 12-mm perivascular probes with a T206 flowmeter; Transonic Systems, Ithaca, NY) were placed around the superior (SVC) and inferior vena cava (IVC) ~1 cm from the caval-atrial junction to measure RA inflow. Micromanometer-tipped pressure catheters (Millar Instruments, Houston, TX) were zeroed in a 37°C water bath for 30 min before insertion. A 1-cm incision was made in the pericardium over the anterior RV free wall, and a 7-Fr micromanometer was positioned in the mid-RV cavity to record RV pressure (RVP). A second 1-cm incision was made in the pericardium over the RA appendage, and a 6-Fr combined pressure-volume conductance catheter (Millar SPR-766) was positioned along the long axis of the right atrium so that its tip rested at the RA-IVC junction. This catheter was connected to a signal conditioner processor (Sigma SDF; CD Leycom, Zoetermeer, The Netherlands) to convert instantaneous conductance measurements into relative RA volume as previously described (24).

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A micromanometer 2 cm from the distal end of the catheter allowed simultaneous measurement of RA pressure (RAP). A tourniquet was positioned around the distal main pulmonary artery (PA) to permit acute RV afterload manipulation via partial PA occlusion. A third 1-cm incision was made over the AV groove to place a vascular loop around the coronary sinus so that it could be occluded during data collection to prevent coronary venous return.

Experimental protocol. With the pericardium intact, data were recorded during steady-state baseline conditions. Between 3 and 10 steady-state beats were recorded during each study intervention, and data acquisition runs were repeated in triplicate. To alter inotropic state, a calcium chloride bolus (10 mg/kg iv) was given, and steady-state data were obtained. Acute pulmonary hypertension was created by partial PA occlusion to produce a 50% rise in maximum RVP, and steady-state data were recorded. The PA tourniquet was released, and RVP returned to its baseline level. After a 10-min stabilization period, the pericardium was opened, and data were again recorded during steady-state conditions. Complete data with the pericardium intact were available in 9 of the 11 animals, and complete data with the pericardium open were available in 7 of the 11 animals. At the conclusion of the experiment, the animals were euthanized using pentothal sodium (1 g iv) followed (after 2 min) by potassium chloride (80 meq iv), and proper positioning of the catheters was confirmed. All animals received humane care in compliance with the “Principles of Laboratory Animal Care” formulated by the National Society for Medical Research and the “Guide for the Care and Use of Laboratory Animals” prepared by the National Academy of Sciences and published by the National Institutes of Health. The study was approved by the Washington University School of Medicine Animal Studies Committee and conducted according to Washington University policy.

Data analysis. During each data acquisition run, ECG, RAP, RVP, SVC flow, IVC flow, and RA conductance signals were acquired at 200 Hz and processed using custom-designed computer software. The RAP and RVP signals were differentiated with respect to time to calculate maximum RA change in pressure over time (dp/dr) and RV dP/dt, and relative RA volume was determined using the conductance catheter as previously described (24, 35). The instantaneous pressure gradient across the tricuspid annulus (RVP-RAP gradient) was corrected for differences in the height of the RAP and RVP sensors (hydrostatic pressure gradient) (20). The average hydrostatic pressure gradient (∆PH) was calculated as the difference between RAP and RVP at the time immediately before the electrocardiographic P wave (during diastasis) and then subtracted from the pressure differential as follows: RVP-RAP gradient = RVP(t) − RAP(t) − ∆PH.

RA reservoir and conduit function. Reservoir and conduit functions of the right atrium were calculated by integrating RA inflow (combined SVC and IVC flow) during RV systole (reservoir) and RV diastole (conduit) (16, 17, 30). Because the tricuspid valve is closed during RV systole, all blood that enters from the cavae during this period is reserved in the atrium (coronary sinus return was temporarily interrupted during data collection). Thus RA reservoir volume equals integrated RA inflow from the ECG R wave to the time of maximum RA volume, which corresponds to the initiation of RA emptying and approximates the time of tricuspid valve opening (17). In contrast, RA conduit volume equals integrated RA inflow during RV filling when the tricuspid valve is open. Total conduit volume was separated into an early component, from the time of maximum RA volume to the beginning of atrial contraction (A wave, time of maximum RA dp/dr), and a late component, from the A wave to the end of RV filling (ECG R wave). The late-conduit component quantifies blood entry into the atrium against the force of the RA kick. Figure 1 illustrates typical hemodynamic data obtained from one animal at baseline. Integrated RA inflow volume during the reservoir and conduit phases was divided by total RA inflow volume (stroke volume) to yield reservoir and conduit (both early and late) function as a percentage of total RA inflow.

### Statistical analysis

All data are reported as means ± SD. Hemodynamic data obtained during steady-state baseline conditions with the pericardium closed and after calcium chloride bolus, partial PA occlusion, and pericardiectomy were compared using repeated-measures ANOVA. When indicated by a significant F statistic (P < 0.05), differences were isolated using Fishers protected least significant difference test. Multiple linear regression analysis was used to determine which hemodynamic factors most influenced reservoir and conduit function, and linear regression was used to determine the relationship between the conduit-to-reservoir ratio and cardiac output (stroke volume times heart rate). All statistical analyses were performed using SigmaStat 2.03 (SPSS, Chicago, IL).

### RESULTS

Table 1 summarizes the steady-state hemodynamic data during baseline (pericardium closed), inotropic stimulation (calcium chloride bolus), and partial PA occlusion and after pericardiectomy. With inotropic stimulation, maximum RVP increased by 38% (P < 0.04), RV dp/dr increased by 26% (P > 0.05), and there was a tendency for RA dp/dr to rise (P = 0.06). With partial PA occlusion, maximum RVP similarly increased by 51% (P < 0.004), but the changes in RV dp/dr and RA dp/dr did not reach statistical significance (P = 0.10 and P = 0.09, respectively). After a pericardiectomy was performed, maximum RV dp/dr fell by 20% (P = 0.06). There were no significant changes with any intervention in heart rate (P > 0.60), P-R interval (P > 0.13), RA filling time (reservoir time, P > 0.75), RA emptying time (total conduit time, P > 0.96), mean RAP (P > 0.28), total RA inflow (stroke volume, P > 0.40), or cardiac output (P > 0.32).

Table 2 and Figs. 2 and 3 summarize changes in reservoir and conduit function with each intervention. At baseline with the pericardium closed, reservoir function accounted for 0.56 (SD 0.13) of RA inflow [21.1 ml (SD 6.8)], early conduit...
function for 0.29 (SD 0.07) [11.2 ml (SD 5.5)], and late conduit function to 0.09 (SD 0.04) did not reach statistical significance (P = 0.09). With partial PA occlusion, early conduit function fell by 31% (P < 0.04) and there was a tendency for reservoir function to increase (P = 0.16) did not significantly influence reservoir and conduit function. Significant factors included RAP (P < 0.004), RVP (P < 0.003), and the RVP-RAP gradient (P < 0.004) at the time of maximum RA volume, which corresponds to the initiation of RA emptying. Table 3 summarizes the impact of each significant factor on reservoir, early conduit, and late conduit function. The cutoff values analyzed include RAP at 0.6 ml, RVP at maximum RA volume, and RVP-RAP gradient at maximum RA volume = 0.53 mmHg, representing the median value for each parameter across all interventions in all animals. With increased RAP at maximum RA volume, reservoir function rose by 12% (P < 0.001) and early conduit function fell by 25% (P < 0.001), resulting in a fall in the early conduit-to-reservoir ratio from 0.43 (SD 0.50) to 0.64 (SD 0.69) (P < 0.004). In contrast, with elevated RVP at maximum RA volume, reservoir function fell by 8% (P < 0.02) and early conduit function rose by 23% (P > 0.006), resulting in a rise in the early conduit-to-reservoir ratio from 0.43 (SD 0.49) to 0.62 (SD 0.69) (P < 0.02). The RVP-RAP gradient at maximum RA volume had a similar effect, increasing the early conduit-to-reservoir ratio from 0.42 (SD 0.50) to 0.64 (SD 0.69) (P < 0.004).

**DISCUSSION**

Previous studies have demonstrated that pericardial integrity can have a profound effect on the interplay between various cardiac chambers and, when lost, can decrease the adaptive capacity of the atrium to stress (1, 3, 11, 16). In an earlier report from this laboratory (24), it was noted that RA contractility (atrial kick) fell by 54% and RA compliance rose by 39% after pericardiectomy. In the current study, without pericardial restraint, the atrium acted more as a reservoir than a conduit; the RA early conduit-to-reservoir ratio fell from 0.56 (SD 0.22) to 0.21 (SD 0.15) (P < 0.006). Likely, the pericardium has a greater effect on the thin-walled atria than on the thick-walled atrioventricular junction, contributing to the marked effect of pericardial integrity on atrial function.

Table 2. Effects of inotropic stimulation with calcium chloride, acute partial PA occlusion, and pericardiectomy on RA reservoir and conduit function

<table>
<thead>
<tr>
<th>Pericardium Closed</th>
<th>Baseline</th>
<th>Calcium</th>
<th>PA occlusion</th>
<th>Pericardium Open Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reservoir volume, ml</td>
<td>21.1 (SD 6.8)</td>
<td>23.2 (SD 6.7)</td>
<td>21.5 (SD 4.3)</td>
<td>27.4 (SD 3.9)</td>
</tr>
<tr>
<td>Early conduit volume, ml</td>
<td>11.2 (SD 5.3)</td>
<td>11.9 (SD 6.0)</td>
<td>7.0 (SD 4.7)*</td>
<td>5.8 (SD 4.3)*</td>
</tr>
<tr>
<td>Late conduit volume, ml</td>
<td>5.3 (SD 2.4)</td>
<td>3.9 (SD 1.0)*</td>
<td>5.4 (SD 1.3)</td>
<td>5.9 (SD 2.6)*</td>
</tr>
<tr>
<td>Reservoir function</td>
<td>0.56 (SD 0.13)</td>
<td>0.63 (SD 0.10)</td>
<td>0.64 (SD 0.08)</td>
<td>0.72 (SD 0.08)*</td>
</tr>
<tr>
<td>Early conduit function</td>
<td>0.29 (SD 0.07)</td>
<td>0.29 (SD 0.11)</td>
<td>0.20 (SD 0.11)*</td>
<td>0.14 (SD 0.09)*</td>
</tr>
<tr>
<td>Late conduit function</td>
<td>0.16 (SD 0.11)</td>
<td>0.09 (SD 0.04)</td>
<td>0.17 (SD 0.06)</td>
<td>0.15 (SD 0.07)</td>
</tr>
<tr>
<td>Early conduit-to-reservoir</td>
<td>0.56 (SD 0.22)</td>
<td>0.50 (SD 0.26)</td>
<td>0.33 (SD 0.22)*</td>
<td>0.21 (SD 0.15)*</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 9 for pericardium closed and 7 for pericardium open. *P < 0.05 vs. pericardium closed baseline. Repeated-measures ANOVA was used for all comparisons.
ventricles. Nagano et al. (28) found in normal subjects that the left atrium was less compliant than the left ventricle, facilitating blood transfer between the chambers during the early conduit phase. It is not surprising, however, that others have suggested that increased atrial compliance, which promotes reservoir function (17, 37), would have a greater positive impact on cardiac output than would supplementation of conduit function (2, 36). Hoit and Gabel (14) examined left atrial mechanics during left ventricular dysfunction, comparing the compensatory response with a normal atrium versus a failing atrium (induced with rapid atrial pacing). With a normal atrium, reservoir function increased by 19% and booster pump function (atrial contraction) nearly doubled to maintain cardiac output despite a fall in left ventricular ejection fraction from 0.57 to 0.32. In contrast, with a failing atrium, reservoir function fell by 30%, conduit function increased by 33%, and the atrial kick disappeared. The shift from reservoir to conduit function in Hoit and Gabel’s study was inadequate to maintain cardiac output, which fell by 20%. In the current study, cardiac output was inversely related to the conduit-to-reservoir ratio, increasing as the reservoir contribution increased ($P < 0.03$). These findings support the theory of Suga and others that a “flexible atrium” would substantially improve the heart’s output (2, 16, 33, 36, 38).

The proper physiological explanation of right heart AV valve mechanics is that the valve leaflets open when ventricular pressure drops below atrial pressure and coapt and close when ventricular pressure exceeds atrial pressure during systole (9, 39). In the current study, RA volume reached its maximum and began to fall when the RVP-RAP gradient was 0.53 mmHg on average. It is important to note, however, that the time of maximum RA volume does not necessarily correspond to the time of tricuspid valve opening. On the left side of the heart, Karlsson et al. (21), using myocardial markers on the mitral valve, demonstrated that the mitral valve moves toward its

Table 3. Effects of RA and RV hemodynamics at the time of maximum RA volume on RA reservoir and conduit function

<table>
<thead>
<tr>
<th></th>
<th>Reservoir</th>
<th>Early Conduit</th>
<th>Late Conduit</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA pressure at maximum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA volume</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4.2 mmHg</td>
<td>0.58 (SD 0.18)</td>
<td>0.28 (SD 0.16)</td>
<td>0.15 (SD 0.13)</td>
</tr>
<tr>
<td>&gt;4.2 mmHg</td>
<td>0.65 (SD 0.15)*</td>
<td>0.21 (SD 0.11)*</td>
<td>0.15 (SD 0.12)</td>
</tr>
<tr>
<td>RV pressure at maximum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA volume</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5.8 mmHg</td>
<td>0.64 (SD 0.16)</td>
<td>0.22 (SD 0.12)</td>
<td>0.15 (SD 0.15)</td>
</tr>
<tr>
<td>&gt;5.8 mmHg</td>
<td>0.59 (SD 0.17)*</td>
<td>0.27 (SD 0.16)*</td>
<td>0.15 (SD 0.09)</td>
</tr>
<tr>
<td>RV-RV pressure at maximum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA volume</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.53 mmHg</td>
<td>0.66 (SD 0.14)</td>
<td>0.22 (SD 0.12)</td>
<td>0.13 (SD 0.10)</td>
</tr>
<tr>
<td>&gt;0.53 mmHg</td>
<td>0.57 (SD 0.18)*</td>
<td>0.27 (SD 0.16)*</td>
<td>0.17 (SD 0.14)*</td>
</tr>
</tbody>
</table>

Values are means ± SD; $n = 254$ including all baseline, calcium chloride, and partial PA occlusion runs with and without pericardial integrity. *$P < 0.05$ for higher values vs. lower values. ANOVA was used for all comparisons.
occlusion, the early conduit-to-reservoir ratio fell from 0.56 to 0.40. The redistribution of conduit to reservoir function during partial PA occlusion, in which the atrium has not had time to adapt, and the elastic recoil stored during the reservoir phase may not be adequate to support ventricular filling. Potentially through a rise in RV suction, the ventricle could actively draw blood into itself through the atrium directly from its inflow source, the systemic venous circulation, expressed as an increase in RA early conduit function. Pressure clamping studies on the right side of the heart would be necessary to prove these theories (19, 20, 27, 29).

Nishikawa et al. (30) demonstrated that with exercise, left atrial reservoir function increased by 37% and left atrial conduit function decreased by 23%. Although Nishikawa et al. did not measure PA pressures, others have demonstrated that substantial pulmonary hypertension can develop during exercise, especially in subjects with abnormal hearts (7, 18, 23, 32). For example, in heart transplant recipients, Pfugfelder et al. (32) noted that peak exercise produced a 90% increase in mean PA pressure with a threefold rise in RAP. In the current study, when RAP at the time of maximum RA volume exceeded 4.2 mmHg, reservoir function rose by 12%, early conduit function fell by 25%, and the early conduit-to-reservoir ratio decreased from 0.65 to 0.40. The redistribution of conduit to reservoir function during exercise was similar to the findings of the current study during partial PA occlusion, in which the atrium acted more as a reservoir than a conduit. With partial PA occlusion, the early conduit-to-reservoir ratio fell from 0.56 (SD 0.13) to 0.33 (SD 0.22) \((P < 0.03)\). Grant et al. (10) demonstrated that the left atrium acts as a short-term storage reservoir and that atrial reservoir function is four times more important than active atrial contraction in providing energy for the work of ventricular filling. Reservoir function also provides capacitance to dampen irregularities of atrial filling and prevent acute elevations of central venous pressure. With chronic exposure to elevated pulmonary pressures, changes in the biochemical properties and myocardial fiber structure of the right atrium likely occur to make it a more efficient capacitor, but future studies are necessary to delineate the mechanistic adaptive response of the right atrium to chronic pulmonary hypertension (6, 22).

**Potential limitations.** As with all open-chest physiology studies in anesthetized animals, there are potential difficulties in translating results to the closed-chest human clinical setting. However, pericardial integrity was maintained through most of the preparation in an attempt to best mimic the natural in vivo state, and although pericardial pressures were not measured, we suspect that the use of transmural pressures (subtracting pericardial pressure from intracavitary pressure) would have demonstrated similar results. In addition, although this study examined only subjects with acute pulmonary hypertension, we anticipate that subjects with chronic pulmonary hypertension and other diseases that impair the right heart may be even more dependent on the atrium’s ability to vary function more as a reservoir or a conduit.

Although we did not quantify booster pump function (atrial contraction) in the current report, its contribution to ventricular filling and cardiac output can be quite important. Active atrial contraction increases stroke volume by 10–20% (30, 34), a contribution that increases via the Frank-Starling mechanism after ventricular ischemia (25) and becomes more important to maintain filling with advanced age and when the ventricle either dilatates or hypertrophies (14, 34). Work at this laboratory has previously shown (24) that atrial contraction increases with acute pulmonary hypertension to support ventricular filling but fails when pericardial integrity is lost. The late conduit phase reported in the current study quantifies RA inflow during atrial contraction. On the left side of the heart, reversed flow is common in the pulmonary veins during the atrial kick, but it disappears with exercise (30). Nishikawa et al. (30) found that the minimum pulmonary venous flow rate rose progressively with increasing levels of exertion. In the current report examining the right side of the heart, reversal of flow in the vena cavae was rare, occurring during the late conduit phase in only 29 of 653 (4%) steady-state beats and more often during inotropic stimulation (7 of 45 beats, 16%) and partial PA occlusion (12 of 166, 7%) than during baseline with the pericardium closed (8 of 267, 3%) or open (2 of 175, 1%).

In summary, this study demonstrated that the right atrium adjusts its ability to act more as a reservoir versus a conduit in a dynamic manner, dependent not only on global physiological changes but also on beat-to-beat changes in the pressure differential between the right-sided chambers. The RA conduit-to-reservoir ratio was directly related to the RVP-RAP gradient at the time of maximum RA volume, with increased ventricular pressures favoring conduit function, but it was inversely related to cardiac output, with an increase in the reservoir contribution favoring increased cardiac output. Although this study examined subjects exposed to acute physiological changes, we anticipate an even more profound impact of RA reservoir and conduit function on RV filling and cardiac output during chronic disease states that impair right heart mechanics.

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