First-in-human experience with occlusion of the superior vena cava to reduce cardiac filling pressures in congestive heart failure

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Abstract

Background: Acutely decompressed heart failure remains a major clinical problem. Volume overload promotes cardiac and renal dysfunction and is associated with increased morbidity and mortality in heart failure. We hypothesized that transient occlusion of the superior vena cava (SVC) will reduce cardiac filling pressures without decreasing cardiac output or systemic blood pressure. The objective of this proof of concept study was to provide initial evidence of safety and feasibility of transient SVC occlusion in patients with acutely decompressed heart failure and reduced ejection fraction.

Methods and Results: In eight patients with systolic heart failure, SVC occlusion was performed using a commercially available occlusion balloon. Five minutes of SVC occlusion reduced biventricular filling pressures without decreasing systemic blood pressure or total cardiac output. In three of the eight patients, a second 10-minutes occlusion had similar hemodynamic effects. SVC occlusion was well-tolerated without development of new symptoms, new neurologic deficits, or any adverse events including stroke, heart attack, or reported SVC injury or thrombosis at 7 days of follow up.

Conclusion: We report the first clinical experience with transient SVC occlusion as a potentially new therapeutic approach to rapidly reduce cardiac filling pressures in heart failure. No prohibitive safety signal was identified and further testing to establish the clinical utility of transient SVC occlusion for acute decompressed heart failure is justified.

KEYWORDS
hemodynamics, new devices (in general), vena cava

1 | INTRODUCTION

By the year 2030, nearly 8 million individuals will have heart failure in the United States alone.1 Reducing ventricular wall stress by decreasing cardiac preload is a cornerstone of management for patients with acute congestive heart failure. The Frank-Starling mechanism identifies preload as a major determinant of cardiac output and further suggests that reducing volume overload may improve cardiac output, or at least not diminish cardiac output, among patients with systolic heart failure in a volume-overloaded state.2 More recent data suggests that elevated cardiac filling pressures are associated with poor short- and long-term outcomes among patients with heart failure.3−5 Current approaches to reduce
cardiac preload focus on diuretic therapy and vasodilators. Device-based approaches for decongestion of patients with acute heart failure include aquapheresis, hemodialysis, and investigational approaches such as impeller pumps in the descending aorta. No existing device is designed to specifically reduce cardiac preload as a method to unload the heart due to a concern that this approach may decrease cardiac output and systemic blood pressure. As nearly one-third of venous return is delivered to the heart via the superior vena cava (SVC), we postulated that temporary occlusion of the SVC may rapidly reduce intracardiac filling pressures without decreasing systemic blood pressure or cardiac output. No prior study has explored the effect of temporary SVC occlusion in patients with heart failure. To test this hypothesis, we performed a single-center, proof of concept study to provide initial evidence of safety, feasibility, and acute hemodynamic effects of transient, catheter-based SVC occlusion in patients with acutely decompensated heart failure.

2 METHODS

2.1 Study population

Patients over 18 year of age admitted with New York Heart Association (NYHA) Class III-IV with a left ventricular ejection fraction <40% and evidence of volume overload referred for right heart catheterization were eligible for inclusion. Patients with acute coronary syndromes, cardio- genic shock, mechanical circulatory support, prior orthotopic heart transplantation, recent stroke, cardiac arrest or cardiac surgery, or history of deep venous thrombosis were excluded. The Institutional Review Board at Tufts Medical Center approved the study. An independent data safety monitor (AW) reviewed each case during execution of the study.

2.2 Study procedures

All patients provided informed consent prior to entry into the catheterization laboratory. After initial hemodynamic assessment using a pulmonary artery catheter, SVC venography was performed and a 32 cc endovascular balloon (Cook Medical) was deployed via the right internal jugular vein or right femoral vein and inflated to occlude the SVC for a total of 5 or 10 minutes (Figure 1A,B). SVC balloon deployment was performed via a separate venous access site from the pulmonary artery catheter to allow for hemodynamic data acquisition during balloon occlusion. Pulmonary artery catheter data and noninvasive systemic blood pressure were measured at baseline, at 1-minute intervals during occlusion, and 5 minutes after release of occlusion. A venogram performed after release of occlusion confirmed SVC integrity. Independent safety monitors adjudicated each case for a decrease in systemic blood pressure by >20 mm Hg or >20% from baseline, elevated jugular venous pressures (JVPs) over 50 mm Hg, vascular injury, or new neurologic symptoms including headache or visual impairment. Patients underwent neurologic testing by a board-certified neurologist before, during, and after SVC occlusion, including quantification of Mini-Cog and National Institutes of Health Stroke Scale (NIHSS) scores. Repeat neurologic testing was performed within 10 minutes of balloon release, and after 1, 3, and 24 hours.

2.3 Statistical analysis

Results are presented as mean ± SD. Paired and unpaired student’s t-tests or one-way ANOVA were used to compare continuous variables between groups using GraphPad Software (La Jolla, California). An alpha-level of P < .05 was considered to indicate a significant effect or between-group difference.

3 RESULTS

A total of eight patient were enrolled and completed the study protocol after providing informed consent. Mean age of study participants was 61 ± 6 years and all patients were male. Mean body surface area was 2.0 ± 0.2 m². Average NYHA class was 3.6 ± 0.5. Ischemic cardiomyopathy was diagnosed in 5 (63%) of patients. Mean LV ejection fraction was 19 ± 10% and LV end-diastolic diameter was 5.9 ± 1.1 cm. Two patients were receiving inotropic support prior to enrollment. All patients were being actively treated with diuretic therapy (furosemide or bumetanide). Mean blood urea nitrogen and creatinine levels were 45 ± 19 ng/dL and 1.5 ± 0.7 ng/dL prior to enrollment. Mean SVC diameter was 24 ± 3 mm.

![Figure 1](wileyonlinelibrary.com)
SVC occlusion was successfully performed for 5 minutes in all patients (Figure 1). Right internal JVP rose from 17 ± 5 to 39 ± 10 mm Hg \((P = .001)\) at 5 minutes and returned to baseline values \((16 ± 6, p = NS vs \text{baseline})\) after release of SVC occlusion. Compared to baseline, 5 minutes of SVC occlusion significantly reduced right atrial pressure \((RA; 19 ± 9 vs 9 ± 4 \text{ mm Hg}, P < .01)\), pulmonary artery systolic pressure \((54 ± 12 vs 35 ± 15 \text{ mm Hg}, P < .01)\), pulmonary artery diastolic pressure \((26 ± 12 vs 15 ± 11 \text{ mm Hg}, P < .01)\), mean pulmonary artery pressure \((\text{mean PA;} 40 ± 12 \text{ to } 24 ± 12 \text{ mm Hg}, P < .01)\) and pulmonary capillary wedge pressure \((29 ± 11 \text{ vs } 13 ± 10 \text{ mm Hg}, P < .01)\) without changing systemic mean arterial pressure \((\text{MAP;} 99 ± 15 \text{ vs } 94 ± 18 \text{ mm Hg}, p = NS)\) or cardiac output \((\text{CO;} 4.4 ± 1.0 \text{ vs } 4.2 ± 1.0 \text{ mm Hg}, p = NS; \text{Figure 2A,B})\). After successful completion of the first five patients, two successive SVC occlusions were performed for 5 and 10 minutes, respectively, in

![Acute hemodynamic effects of superior vena cava (SVC) occlusion in heart failure. A, Box plots of hemodynamic variables including heart rate (HR); mean arterial pressure (MAP), jugular venous pressure (JVP), right atrial (RA), mean pulmonary artery (mPA), and pulmonary capillary wedge pressure (PCWP) before, during and after 5 minutes of SVC occlusion. B Individual line plots for the eight enrolled patients showing that 5 minutes of SVC occlusion reduces cardiac filling pressures without affecting systemic MAP.](image-url)
patients 6, 7, and 8. Hemodynamic indices with 10 minutes of SVC occlusion were similar to 5 minutes of occlusion with reduced cardiac filling pressures, stable MAP, and elevated JVP that recovered to baseline after release of the SVC occlusion.

Neurologic testing was performed before and after sedation in the catheterization laboratory, before and after each SVC occlusion, and at 1, 3, and 24 hours after completion of the SVC occlusion procedure. No patients complained of new symptoms including headache, visual disturbance, head or neck fullness, tongue swelling, or change in swallowing or speech during or after SVC occlusion. Mini-Cog and NIHSS scores were unchanged compared to baseline values for all patients (Figure 3). At 7 days of follow up, all patients were alive without stroke, heart attack, reported SVC injury or thrombosis, and without unanticipated surgery.

4 | DISCUSSION

We report the first-in-human experience with SVC occlusion as a potentially novel therapeutic approach to rapidly and significantly reduce cardiac filling pressures in acutely decompensated systolic heart failure. SVC occlusion was well-tolerated with stable MAPs and cardiac output, and without neurologic side effects. Future studies are justified to determine the clinical utility of SVC occlusion as an approach to improve outcomes for patients with acute decompensated congestive heart failure.

Successful completion of this proof of concept study allows for development of novel therapeutic approaches to simultaneously unload the right and left heart among patients with heart failure. Several mechanisms may explain the potential benefit of intermittent SVC occlusion in heart failure. First, reducing cardiac preload by one-third decreases biventricular pressure and volume. This unloading effect reduces cardiac workload, oxygen consumption, and promotes rapid decongestion of both the pulmonary and systemic venous circuits. At present, rapid ventricular unloading can only be achieved with the use of complex rotary flow pumps. Second, we also know from the Frank-Starling mechanism that patients with systolic heart failure are particularly sensitive to volume overload, which may further dilate the left ventricle and stretch cardiac myocytes, thereby further impairing contractility. By partially reducing LV volume, contractility may increase thereby sustaining and potentially increasing cardiac output. Third, patients with elevated right and left heart filling pressures may benefit from SVC occlusion because a reduction in right ventricular pressure and volume overload may cause the interventricular septum to shift toward the right ventricle, thereby increasing LV capacitance and stroke volume. Fourth, elevated central venous pressure is associated with renal, hepatic, and bowel congestion. Systemic venous congestion has been associated with impaired renal function and diuretic resistance. Decompression of central venous pressure may promote renal function and improve diuretic responsiveness, thereby leading to earlier decongestion of patients with acutely decompensated heart failure. This early proof of concept study is the first to identify that simply inflating a balloon and temporarily occluding flow in the SVC rapidly decompresses both the right and left ventricles without reducing systemic blood pressure or decreasing cardiac output. To achieve the potential benefits of SVC occlusion as a therapy for heart failure, a system that intermittently occludes the SVC may be required. Intermittent SVC occlusion may include a duty cycle that functions similar to an intra-aortic balloon pump, however instead of rapid inflation and deflation of a balloon in concert with heart rate, an SVC occlusion system could inflate for a period of minutes, then transiently deflate to allow for flow through the SVC. No prohibitive safety signals were identified in this proof of concept study to preclude further investigation of intermittent SVC occlusion as a therapeutic approach for congestive heart failure.

Figure 3

No prior reports have tested SVC occlusion as a therapeutic approach to reduce cardiac filling pressures in heart failure. In this study, balloon positioning in the SVC was favored over inferior vena caval (IVC) occlusion for several reasons. First, the IVC provides nearly two-thirds of cardiac preload. Complete occlusion of the IVC leads to profound hypotension within minutes due to magnitude of preload reduction and is commonly used to establish end-systolic pressure-volume relationships by evacuating the LV of volume. Second, IVC occlusion may increase hepatic, portal, or renal vein pressure, thereby potentially increasing kidney and hepatic injury in heart failure. Third, IVC occlusion may promote venous congestion of the bowel thereby reducing absorption of orally prescribed drugs. For these reasons, occlusion of the SVC was considered superior to IVC occlusion.

One potential concern associated with SVC occlusion is an acute increase in JVP. No studies have tested the impact of temporary SVC occlusion on cerebral perfusion. More commonly, SVC occlusion has been studied in the context of SVC syndrome—a chronic, acquired condition whereby flow through the SVC is restricted due to extrinsic compression or intraluminal thrombus. In these cases, collateral flow through venous and lymphatic vessels provides an alternative route to...
the right atrium, thereby preserving cardiac preload. In the setting of chronic SVC occlusion, four collateral venous systems include: the azygous-hemiazygous, the internal mammary-epigastric, the lateral thoracic, and the innominate-vertebral pathways. In contrast, few studies describe the clinical use of SVC occlusion, which is more commonly described in association with SVC balloon inflation or stenting for the treatment of SVC syndrome. None of these studies report any neurologic deficit due to SVC occlusion. In this proof of concept study, all patients presented with elevated jugular vein pressure, which increased during SVC occlusion. Rigorous neurologic testing was performed and did not identify any neurologic risk during or up to 7 days after SVC occlusion.

Our study has several limitations. First, the number of patients studied is small. To establish safety, feasibility, and potential efficacy a larger, more intensive study is required. Second, we only tested transient SVC occlusion for 5 or 10 minutes. To identify any durable benefit in terms of improved symptoms, cardiac function, or diuretic responsiveness, a more prolonged therapy is required. A prospective study testing a new device-based approach to intermittent occlusion of the SVC is in development.

In conclusion, we report the first clinical proof-of-concept results with transient SVC occlusion as a potentially new therapeutic approach to rapidly reduce cardiac filling pressures in heart failure. No prohibitive safety signal was identified and further testing to establish the clinical utility of transient SVC occlusion for heart failure is required.

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DISCLOSURES


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