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Evaluation of Right Atrial-Coronary Sinus Pressure Gradients in Patients with Left Ventricular Dysfunction Undergoing Defibrillator Implantation. Description of the Phenomenon of Coronary Sinus Flow Reversal and its Incidence

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ABSTRACT

We have previously reported that during coronary sinus venography there can be reflux of dye from the coronary sinus ostium towards the distal part of the sinus against the anticipated direction of flow. This phenomenon appeared to be unrelated to the cardiac cycle or respiratory cycle. We postulated that variations in the pressure gradient between the right atrial pressure and coronary sinus pressure (CSp) are responsible for the observed phenomenon. Additionally, we postulated that this phenomenon may predict heart failure progression in patients with left ventricular (LV) dysfunction. A prospective, randomized study was performed with forty-seven patients who were undergoing ICD implant (single, dual chamber or CRT). Prior to lead placement, pulmonary artery pressure (PAp), CSp, and right atrial pressure (RAp) were recorded simultaneously during inspiration and expiration. Patients were categorized in high or low Pap groups (> 45 or ≤ 45 mm Hg). A trend towards increased CSp in patients with high PAp was observed as well as a pressure gradient reversal (RAp > CSp) during inspiration in twenty-four of twenty-nine (83%) patients ranging from 3% to 100% percent time of the cardiac cycle. There are dynamic changes in the RAp and CSp gradients during respiration that can induce reversal of flow gradient even with normal Pap. This may provide a mechanism to explain interventricular interdependence and LV dysfunction in patients with PHT.

***New and Noteworthy:** This is the first description of measurements of pressure gradients between the right atrium and coronary sinus and flow reversal in the coronary sinus in patients with congestive heart failure.*

Keywords

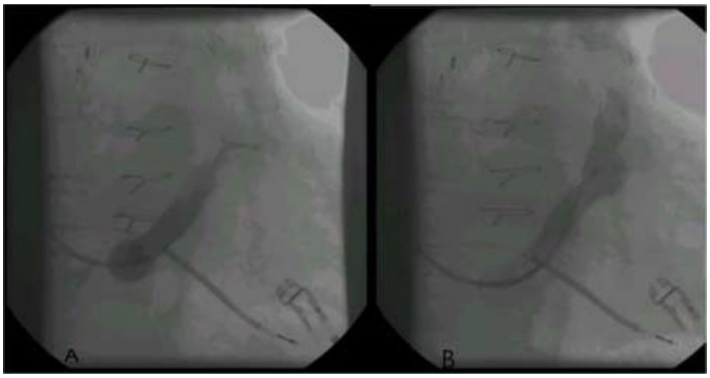
Coronary sinus, Congestive heart failure, Pulmonary Hypertension, Interventricular Inter dependence, Coronary Sinus Flow reversal

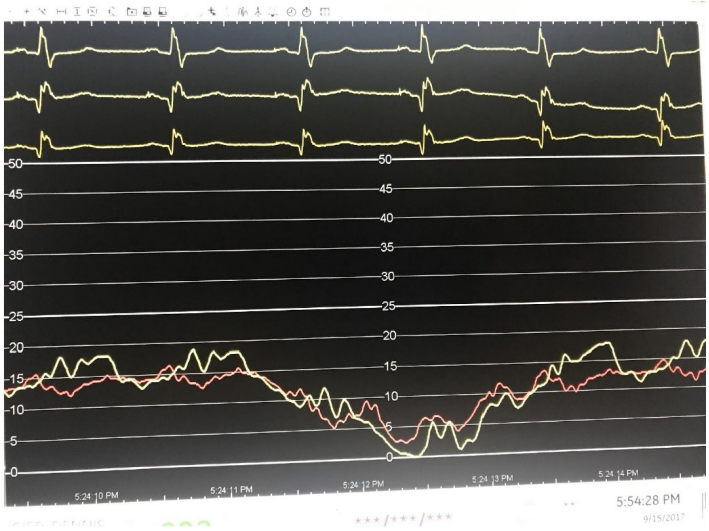
Introduction

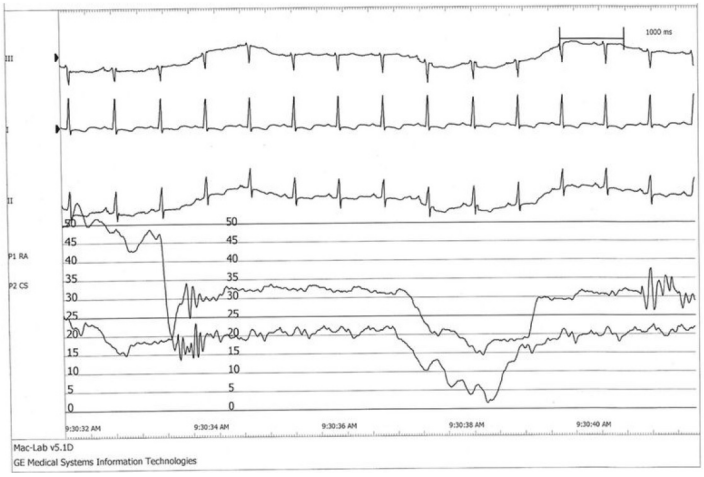
The effects of elevated coronary sinus pressure (CSp) on heart failure progression are largely unknown. We have reported the occurrence of coronary sinus (CS) flow stasis or flow reversal during non-occlusive coronary sinus venography during CRT (Cardiac resynchronization therapy device) implantation. Reversal of coronary sinus pressures may occur due to elevated right atrial pressures above the CS pressure due to a variety of mechanisms. In animal models, elevation of CS pressure can cause diastolic dysfunction by impeding coronary venous flow and possible affecting Left ventricular wall stiffness.

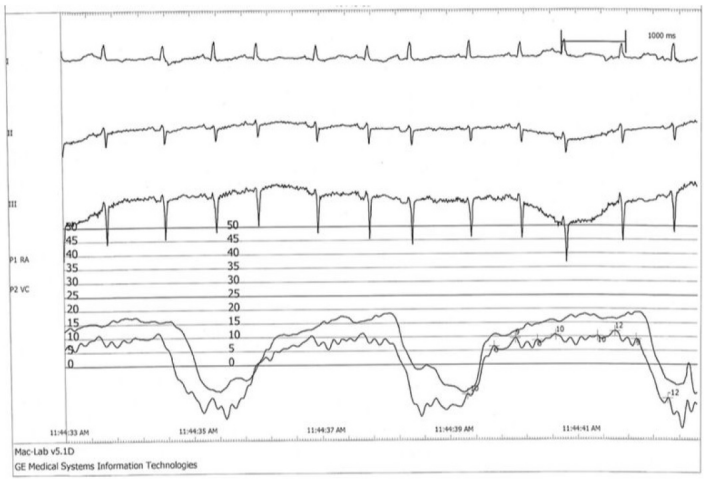
Progressive deterioration of left ventricular (LV) function can be seen sometimes in patients with pulmonary hypertension, which has been previously considered to be secondary to inter-ventricular septum displacement due to right ventricular (RV) enlargement and pressure overload. However, it is possible that CS drainage impairment can be additional mechanism for inter-ventricular interdependence; a mechanism by which worsening right heart function may adversely impact LV function in the failing heart. This may also be an important mechanism by which congestive heart failure progresses.

This study aims to evaluate the incidence of coronary sinus flow reversal, quantify the effects and assess the possibility that this may be related to progression of congestive heart Failure. We measured the pressures in the CS and RA in patients undergoing implantable cardioverter-defibrillator (ICD) implantation or cardiac resynchronization therapy (CRT) device implantation and to investigate how this data relates to patient outcomes. Results from this study may allow identification of the incidence of flow stasis and reversal of CS flow in a CHF population, specifically in patients with underlying pulmonary hypertension.









Methods

This is a prospective, non-randomized study. All participating patients were implanted with an FDA approved AICD (Automatic Implantable cardiac Defibrillator or CRT (Cardiac Resynchronization therapy) device and compatible lead system. Informed consent for pressure measurements and study was obtained from patients prior to device implantation. The study was reviewed and approved by the local Institutional Review Board (Sacred Heart Hospital, Pensacola, FL).

During device implantation, patients underwent simultaneous Right Atrial (RA) and Coronary Sinus (CS) pressure measurements using angiographic catheters (JR4) that were positioned in the RA and CS. CS Sheath was connected to a transducer after dye injection confirmed coaxial sheath placement in the middle part of the CS. Another transducer was connected to a sheath positioned in the mid RA.

Prior to recording, the transducers were calibrated and confirmed to be at the level of the Right atrium (RA). The RA, Right ventricle (RV), Pulmonary artery (PA), and Aortic (Ao) pressures were also measured. Also, simultaneous CS and RA pressures were recorded in a recording system where two simultaneous pressure tracings are stored digitally and printed on paper.

Patients were categorized into one of two groups depending on the PA pressure measurements taken at implant. One group will consist of those patients with a PA pressure ≤ 45 mmHg (n=15) and the other group > 45 mmHg (n=15).

Follow up were performed at one-week post-implant and six-month post implantation of device. At follow up visits, assessment of NYHA class was performed, a 6-minute hall walk test, and complete a Minnesota Living with Heart Failure (MLWHF) questionnaires were completed.

Sample Size

Forty (40) consecutive patients scheduled to undergo ICD or CRT device implantation were enrolled into the study. Twenty patients will be placed in the control group (PA pressure ≤ 45 mmHg),

and twenty patients enrolled in the study group (PA pressure > 45 mmHg).

Inclusion Criteria

Patients were eligible for enrollment if they

- Have a standard indication for an ICD or CRT device.
- Have a history of CHF due to left ventricular dysfunction with or without pulmonary hypertension
- Are willing to comply with follow-up schedule.

Exclusion Criteria

- Patient is unable to comply with the follow-up visits due to geographical, psychological, or any other reasons.
- Patient is younger than 18 years of age.
- Patient is pregnant.
- Patient's life expectancy is less than 6 months.

Enrolment (Implant)

- Prior to enrolment, the patient undergoes an echocardiogram.
- Obtain a non-occlusive coronary sinus venogram and save the images on a CD.
- At implant, measure the PA, RA, RV, Aortic and CS pressures.
- Patients are enrolled in one of two groups; Group A with PA pressures ≤ 45 mmHg, and Group B with PA pressure > 45 mmHg.

1 week post-implant follow up visit

- Based on the PA pressure measurement at implant, the patient should already have been categorized to be in either the control group (PA ≤ 45 mmHg) or the study group (PA >45 mmHg).
- Assess patient's NYHA class.
- Administer a 6-minute hall walk test as described in Appendix A.
- Administer a MLWHF QOL questionnaire to patient.
- Perform standard ICD or CRT system evaluation, which may include capture and sensing thresholds, assessment of high and low voltage impedance, and any other testing deemed appropriate by the investigator.
- Print the final Parameter Summary report.
- Complete the Follow-up Case Report Form and the Medical History and Demographics Case Report Form.

6 months post enrollment ± 4 weeks follow up visit

- Assess patient's NYHA class.
- Administer a 6-minute hall walk test as described in Appendix A.
- Administer a MLWHF QOL questionnaire to patient.
- Print out the following reports:
    a. Parameter Summary
    b. Real-Time Measurement Trends
    c. Tachycardia Diagnostics
    d. Bradycardia Diagnostics
    e. Stored EGM's
- Perform standard ICD or CRT system evaluation, which may include capture and sensing thresholds, assessment of high and low voltage impedance, and any other testing deemed appropriate by the investigator.
- Evaluate stored EGM's for appropriate or inappropriate therapies.
- Record all medications.
- Print the final Parameter Summary report.
- Complete the Follow-up Case Report Form.

Results

Forty seven patients undergoing ICD implant (single, dual chamber or CRT) were enrolled. Forty-four of forty-seven patients (94%) who were able to complete the follow up visits, were included for analysis. Patients were categorized in high PAp groups (> 45 or ≤ 45 mm Hg). Percentage time pressure reversal (RAp > CSp) was obtained by measuring the time that Rap was greater than CSp divided by the cardiac cycle length. Heart failure progression was assessed by NYHA class, Minnesota Living with Heart Failure, and six-minute hall walk test at baseline (< 7 days post implant) and at six months. A trend towards increased CSp in atients with high PAp was observed. A wide range of pressure gradient reversal (RAp > CSp) was seen ranging from 3-100% of the cardiac cycle. We found no significant correlation between the percent time CSp reversal and the heart failure progression.

20.	PA pressure ≤ 45 mmHg (n=24) Group 1	PA pressure > 45 mmHg (n=20) Group 2	P value
Gender	8 % Female	40 % Female	0.01
Systolic Pressure	117.5 ± 17.9 mmHg	126.9 ± 21.5 mmHg	0.1
Diastolic Pressure	70.3 ± 10.2 mmHg	71.1 ± 13.1 mmHg	0.8
Ischemic history	54 %	55 %	0.9
HF history	88 %	75 %	0.3
RA Pressure	14.1 10.4 mmHg	19.8 ± 8.1 mmHg	0.05
RV Pressure	34.6 ± 12.1 mmHg	60.1 ± 11.9 mmHg	<0.001
Aortic Pressure	98.3 ± 41.7 mmHg	121.6 ± 21.6 mmHg	0.03
CS Pressure	16.6 ± 7.8 mmHg	22.2 ± 9.1 mmHg	0.04
CS Flow Reversal	22.24% ± 28.1% (n=14)	36.11% ± 37.1% (n=15)	0.27
LVEF %	28 ± 1.2	27 ± 1.8	0.52

Discussion

As demonstrated by the patients with severe congestive heart failure in these cases, reversal of blood flow in the coronary sinus vein is caused by a pressure gradient from the right atrium to the coronary sinus. Though the mechanisms by which this gradient was maintained is unknown, this phenomenon appears to be promoted primarily by severe tricuspid regurgitation and resultant right atrial hypertension.

There exists evidence of the adverse effects of right atrial and coronary sinus hypertension on the left ventricular collateral circulation and left ventricular function potentially contributing to the progression of congestive heart failure. The pathophysiological consequences of coronary sinus flow reversal are discussed here based upon previously published studies. The treatment of myocardial ischemia by retrograde perfusion

through the coronary sinus has been evaluated in patients with acute myocardial infarction, coronary artery bypass grafting and coronary revascularization [1]. However, there is conflicting data in this regard. It is known that there is no discernible benefit of retrograde coronary sinus perfusion in alleviating ischemia in pigs that do not have performed collaterals [2], which necessitates pre-existing collaterals in order for coronary sinus retrograde perfusion to be of any benefit in preventing ischemia. This leads to the possibility of using coronary sinus obstruction to improve the condition of patients suffering from myocardial ischemia and infarction who have "no reflow." This, however, has been studied and unfortunately could not be applied clinically due to potential venous engorgement, myocardial edema, and injury to coronary veins [3].

During the placement of the left ventricular leads via the coronary sinus, dissection of the coronary sinus often occurs [4]. Though this incidence is reported to be as high as 6.8 % in some series, this is likely due to the older stylet driven leads, and it is likely that with over the wire lead systems the incidence is lower. Though this occurrence of this complication is quite high, patients do not exhibit any symptoms that would indicate cardiac compromise upon the partition of the coronary sinus.

A study was published by Yu et al. regarding the effects of elevated right atrial pressure on blood flow to collateral-dependent and normal myocardium of in-situ hearts in canines with acute occlusion of the left anterior descending coronary artery using radioactive microspheres [5]. Upon constricting the pulmonary artery, they were able to increase the pressure in the right atrium. At a pressure 34 mm Hg, there was no significant effect on blood flow to any transmural region of canine left ventricle. In the instance of increased right ventricular pressure, "vascular waterfalls" supposedly protect the left ventricle from any deleterious effects. A right atrial pressure of 50 mm Hg, however, decreased collateral flow in subepicardial region but increased blood to the subendocardial ischemic tissue. This occurred because venous drainage was redirected into the left ventricular cavity which increases subendocardial blood flow, thus potentially creating a protective effect in the ischemic heart as ischemia tends to be much worse in the subendocardial region of the myocardium. A similar study examined the effects of coronary sinus pressure elevation using coronary sinus occlusion in seven adult ewes placed under Phenobarbital anesthesia [6]. The results of this study did not indicate any significant difference in the blood flow in the endocardial and epicardial areas though coronary sinus pressures in this study were not elevated to a comparably high level as in the aforementioned canine study.

Another study performed consisted of an examination of coronary sinus occlusion in thirty-eight anesthetized dogs that underwent occlusion of the left anterior descending artery and then coronary sinus occlusion [7]. Within twenty-five seconds after occlusion, coronary sinus pressure exceeded 11 mm Hg in all dogs and plateaued at 34 ± 3 mm Hg. 11 mm Hg indicates the approximate threshold level of the pressure of the venous waterfalls [8,9]. The effects of the coronary sinus occlusion on the coronary flow into the non-ischemic region can potentially promote a shift of blood flow to the ischemic region which is exposed to a lower tissue perfusion pressure [10].

Coronary blood flow is thought to follow the principles of a "vascular waterfall phenomenon" [11], which can provide an explanation as to why coronary sinus pressure is not directly transmitted backward into the coronary arteries. This phenomenon suggests that since the blood vessels running along the surface of the heart and through muscle tissue are flexible and thus affected by pressures external to them, they have the potential to collapse if the pressure outside is higher than the pressure at their downstream ends. These collapsed vessels may become Starling resistors or vascular waterfalls. This explains why vascular waterfalls may protect left ventricular arterial flow from the destructive effects of elevated right atrial pressure.

Coronary venous drainage occurs primarily through the coronary sinus into the right atrium. Alternative routes run through the Thebesian veins, which drain directly into the cardiac chambers and the anterior cardiac veins which drain to the right atrium entirely independent of the coronary sinus [12,13].

It is reported that severe acute pulmonary hypertension can affect left ventricular function adversely [14]. Sestier et al. studied the effects of acute right ventricular pressure overload on left ventricular regional blood flow in a canine model. Their results showed that 10 and 30 minutes following the banding of the pulmonary artery, the left ventricular subendocardial:subepicardial ratio dropped by 12 and 31% (p value < 0.05). Though the mechanism by which this occurred was unclear, it is generally accepted that interference with left ventricular function by causing septal flattening in what is described as interventricular interdependence is the result of right ventricular pressure overload [15].

A study entitled "Transesophageal Doppler Analysis of Coronary Sinus Flow A New Method to Assess the Severity of Tricuspid Regurgitation" encompassed an analysis of coronary sinus flow using pulsed-Doppler transesophageal echocardiography in 70 consecutive patients with some degree of tricuspid regurgitation (27 mild, 14 moderate, and 29 severe) and in 35 patients without tricuspid regurgitation [16]. The results revealed that the coronary sinus Doppler flow pattern was a combination of two negative waves, a late systolic wave and another diastolic one with higher velocity and longer duration in patients with mild to no occurrence of tricuspid regurgitation. The systolic wave became reversed in 21 (96%) of the patients with severe tricuspid regurgitation. The sensitivity, specificity, and diagnostic accuracy of the presence of a reversed systolic wave in the coronary sinus for the diagnosis of severe tricuspid regurgitation was 95%, 82%, and 80%, respectively. Despite the indication of systolic flow reversal in the coronary sinus, complete reversal of flow was not observed in this series.

Another study describes a patient with chronic atrial fibrillation

and severe left ventricular dysfunction [17] who was found to have an extensive thrombus in the right atrium and coronary sinus. After a thrombectomy, there was significant and rapid recovery of left ventricular function suggesting an important contribution of coronary sinus thrombosis to the genesis of left ventricular dysfunction.

It is reported that severe pulmonary hypertension can adversely affect left ventricular function. Davis et al. studied the mechanism of left ventricular dysfunction due to pulmonary hypertension in canines that underwent pulmonary banding [18]. The dogs were killed after three hours of pulmonary arterial hypertension or control. The left ventricles were excised to determine wet-to-dry ratios. The results indicated a significantly higher ratio in the pulmonary-artery banded dogs (3.57 ± 0.12) than in the sham-operated dogs (3.41 ± 0.17). They also measured preload recruitable stroke work (an index of contractility) which decreased to 56.8 ± 30.3% of control after three hours of pulmonary hypertension. "Tau", which represents the time constant of isovolumic relaxation- an index of diastolic function) slowed significantly from 29.8 ± 5.8 ms at baseline to 63.6 ± 30.4 ms after three hours of pulmonary arterial hypertension.

The sham-operated dogs showed no differences in these indices, and they concluded that pulmonary hypertension causes left ventricular myocardial interstitial edema, which results in both systolic and diastolic left ventricular dysfunction. A similar study by Pratt et al. [18] evaluated the direct and indirect effects of acute coronary sinus hypertension (CSH) on LV function. The results of this study agreed with the study conducted by Davis et al. that interstitial myocardial edema leads to systolic and diastolic function.

Left ventricular end diastolic pressure was not recorded in our patient, but if it reached the high level often associated with congestive heart failure, then venous blood drainage into the left ventricular cavity would be impaired.

In summary, coronary sinus flow reversal as observed during coronary sinus venography is a complex phenomenon resulting in an array of results. It appears that coronary collateral flow can potentially improve at lower right atrial pressures in certain regions where ischemia is present, and upon critical elevation of coronary sinus pressure, coronary arterial blood flow is supposedly compromised by surpassing the pressure of the venous waterfalls and myocardial tissue. Patients undergoing extensive coronary sinus dissection generally tolerate the condition well suggesting that the coronary venous system has significant flexibility. However, it has been observed that in patients with congestive heart failure and elevated left ventricular pressure, this alternate source of venous drainage may also be impaired which can contribute to increased myocardial interstitial edema, which further worsens left ventricular function. This usually occurs in cases where congestive heart failure has already reached an advanced stage, thus demanding application of a more aggressive therapy specifically aimed at reducing right atrial pressure. It is known that venous engorgement affects myocardial stiffness, and this in turn impacts diastolic and systolic function. The apparent complex interaction of coronary blood flow, presence of collaterals, degree of coronary sinus hypertension, and the degree of elevation of left ventricular end diastolic pressure appears to uniquely determine the symptoms of each individual patient, and therefore coronary sinus flow reversal seems to be a very relevant finding in the presence of congestive heart failure.

References

1. Berland J, Farcot JC, Barrier A, et al. Coronary venous synchronized retroperfusion during percutaneous transluminal angioplasty of the left anterior descending artery. Circulation. 1990; 81: 35-42.
2. Toggart EJ, Nellis SH, Leidtke AJ. The efficacy of intermittent coronary sinus occlusion in the absence of coronary sinus collaterals. Circulation. 1987; 76: 667-677.
3. Mohl W, Faxon D, Glogar D, et al. Report of the international working group on coronary sinus interventions. New approach to Interventional Cardiology, New York Springer-Verlag. 1986; 2-10.
4. de Cock, van Campsen, Visser. Major dissection of the coronary sinus and its tributaries during lead implantation for biventricular stimulation Angiographic follow-up. Europace. 2004; 6: 43-47.
5. Yu, Tune, Downey. Elevated right atrial pressure does not reduce collateral blood lfow to ischemic myocardium. Am J Physiol. 1997; 273: H2296-H2303.
6. Ward, Fisher, Michael. Elevated coronary sinus pressure does not alter myocardial blood flow or left ventricular contractile function in mature sheep. Implications after the Fontan Procedure. J Thorac Cardiovasc Surgery. 1988; 95: 511-515.
7. Ido, Hasebe, Matsuhashi, et al. Coronary Sinus occlusion enhances coronary collateral flow and reduces subendocardial ischemia. Am J Physiol Heart Circ Physiol. 2001; 280: H1361-H1367.
8. Farhi ER, Klocke FJ, Mates RE, et al. Tone dependent waterfall behavior during venous pressure elevation in isolated canine hearts. Circ Res. 1991; 68: 392-401.
9. Uhlig PN, Baer, RW, et al. Arterial and venous coronary pressure flow relations in anaesthetized dogs. Evidence for vascular waterfalls in coronary veins. Cardiovasc Res. 1984; 55: 238-248.
10. Matsuhashi HH, Hasebe N, Kawamura Y. The effect of intermittent coronary sinus occlusion on coronary sinus pressure dynamics and coronary arterial flow. Jpn Circ J. 1992; 56: 272-285.
11. Uhlig, Baer, Vlahakes, et al. Arterial and venous coronary pressure-flow relations in anesthetized dogs. Evidence for a vascular waterfall in epicardial coronary veins. Circ Res. 1984; 55: 238-248.
12. Ratajczyk-Pakalska E, Kolff WJ. Anatomical basis for the coronary venous outflow. New York Springer- Verlag. 1984; 40-46.
13. Scharf Sm, Bromberger-Barnea B, Permutt S. Distribution of Coronary venous flow. J Appl Physiol. 1971; 30: 657-662.

14. Sestier, Mildenberger, Klassen. Redistribution in left ventricular regional blood flow following acute right ventricular pressure overload. Can J Physiol Pharmacol. 1989; 56: 185-190.
15. Ryan T, Petrovic O, Dillon JC, et al. An echocardiographic index for separation of right ventricular volume and pressure overload. J Am Coll Cardiol. 1985; 5: 918-927.
16. Zamorano J, Almerica C, Alfonso F, et al. Transesophageal doppler analysis of coronary sinus flow a new method to assess the severity of tricuspid regurgitation. Echocardiography. 1997; 14: 579-588.
17. Neri E, Tripodi A, Tucci E, et al. Dramatic improvement of LV function after coronary sinus thromboembolectomy. Ann Thorac Surg. 2000; 70: 961-963.
18. Davis KL, Melhorn U, Laine GA, et al. Myocardial edema left ventricular function and pulmonary hypertension. Appl Physiol. 1995; 78: 132-137.
19. Pratt JW, Schertel ER, Schaefer SL, et al. Acute transient coronary sinus hypertension impairs left ventricular function and induces myocardial edema. Am J Physiol. 1996; 271: H834-H841.

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