Retained Blood Syndrome After Cardiac Surgery

A New Look at an Old Problem

Edward M. Boyle, Jr., MD, A. Marc Gillinov, MD,† William E. Cohn, MD,‡ S. Jill Ley, RN,§ Theodor Fischlein, MD,|| and Louis P. Perrault, MD, PhD¶*

Abstract: Retained blood occurs when drainage systems fail to adequately evacuate blood during recovery from cardiothoracic surgery. As a result, a spectrum of mechanical and inflammatory complications can ensue in the acute, subacute, and chronic setting. The objectives of this review were to define the clinical syndrome associated with retained blood over the spectrum of recovery and to review existing literature regarding how this may lead to complications and contributes to poor outcomes. To better understand and prevent this constellation of clinical complications, a literature review was conducted, which led us to create a new label that better defines the clinical entity we have titled retained blood syndrome. Analysis of published reports revealed that 13.8% to 22.7% of cardiac surgical patients develop one or more components of retained blood syndrome. This can present in the acute, subacute, or chronic setting, with different pathophysiologic mechanisms active at different times. The development of retained blood syndrome has been linked to other clinical outcomes, including the development of postoperative atrial fibrillation and infection and the need for hospital readmission. Grouping multiple objectively measurable and potentially preventable postoperative complications that share a common etiology of retained blood over the continuum of recovery demonstrates a high prevalence of retained blood syndrome. This suggests the need to develop, implement, and test clinical strategies to enhance surgical drainage and reduce postoperative complications in patients undergoing cardiothoracic surgery.

Key Words: Bleeding, Tamponade, Postoperative care, Hemothorax, Pleural effusion.

(*Innovations* 2015;10:296–303)

Accepted for publication August 27, 2015

From the *Department of Thoracic Surgery, St. Charles Medical Center, Bend, OR USA; †Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic, Cleveland, OH USA; ‡Department of Cardiovascular Surgery, Texas Heart Institute, Houston, TX USA; §Department of Nursing, California Pacific Medical Center, San Francisco, CA USA; ||Department of Cardiac Surgery, Paracelsus Medical University, Nuremberg, Germany; and ¶Department of Surgery, Montreal Heart Institute, Montreal, QC Canada.

Disclosures: Edward M. Boyle, Jr., MD, is a founder, director and shareholder of ClearFlow, Inc., Anaheim, CA USA. A. Marc Gillinov, MD, is an inventor and consultant with stock options and a royalty from Clearflow, Inc; a consultant to On-X Life Technologies, Inc., Austin, TX USA, and Abbott, Abbott Park, IL USA; has research support from St. Jude Medical, Inc., St. Paul, MN USA; and speaking honoraria for Edwards Lifesciences Corp., Irvine, CA USA, St. Jude Medical, Inc., Medtronic, Inc., Minneapolis, MN USA, Intuitive Surgical, Sunnyvale, CA USA, and AtriCure, Inc., West Chester, OH USA. William E. Cohn, MD is a director at Cardiovascular Systems, Inc, St. Paul, MN USA, TVA Medical Inc., Austin, TX USA, SentreHEART, Inc., Redwood City, CA USA; a shareholder in ClearFlow, Inc.; and is a consultant for Mardil Medical, Minneapolis, MN USA, Sunshine Heart, Inc., Eden Prairie, MN USA, ReliantHeart, Inc., Houston, TX USA, and BiVACOR Inc., Houston, TX USA. S. Jill Ley, RN, has received speaker honoraria from ClearFlow, Inc. Louis P. Perrault, MD, PhD, and Theodor Fischlein, MD, declare no conflicts of interest. The Cleveland Clinic has equity in ClearFlow, Inc., and has received royalties.

Address correspondence and reprint requests to A. Marc Gillinov, MD, Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic, 9500 Euclid Ave, Desk J4-1, Cleveland, OH 44195 USA. E-mail: gillinom@ccf.org.

ISSN: 1556-9845/15/1005-0296

Postoperative bleeding is common in patients recovering from heart surgery.[1,2] Reliable postoperative evacuation of shed blood is imperative during this time frame to facilitate mediastinal decompression and pulmonary reexpansion, particularly in the early hours after surgery. Chest drainage tubes are required to maintain adequate evacuation of shed blood during bleeding episodes. Chest tubes, however, often become occluded by clotted blood, leading to unevacuated retained blood around the heart and lungs. In a survey of cardiothoracic surgeons and specialty cardiac surgery nurses, 100% had seen chest tube clogging in their patients clinically, and a large majority reported adverse events related to retained blood.[3] In a recent prospective observational study, 36% of chest tubes were noted to be occluded after routine heart surgery, and a majority of obstructions were in the part of the chest tube in the chest and therefore unrecognized by intensive care unit (ICU) care providers.[4] Once retained blood clots outside the chest tubes, it accumulates in the pericardial and or pleural spaces and can result in acute mechanical compression of the heart and lungs, or in smaller volumes, it may be a powerful driver of local inflammation within the pericardial and pleural spaces, leading to effusions or late fibrosis.

A more comprehensive and unifying composite description of this clinical entity is needed to better study the incidence and clinical consequences of retained blood over the continuum of recovery and create measureable targets for quality improvement initiatives that improve these outcomes. Considered as a composite, retained postsurgical blood may result in a group of conditions that include interventions for tamponade and/or hemothorax in the acute setting, pericardial and/or pleural effusions subacutely, or fibrosis in the chronic setting. Because this is a collection of conditions over time with a unifying root cause, we term this composite constellation of related complications the retained blood syndrome (RBS) (Fig. 1). The purposes of this review were to define this clinical entity of RBS and delineate its presentation and impact on acute,

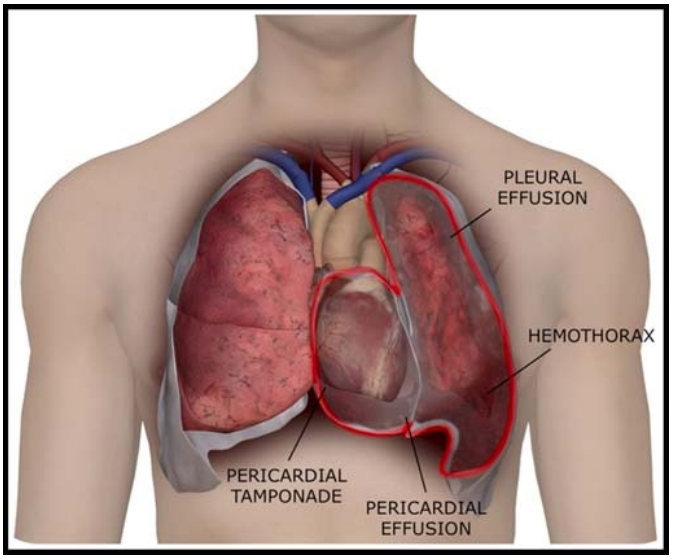

FIGURE 1. Retained blood syndrome includes any combination of hemothorax, pericardial tamponade, pleural effusion, and pericardial effusion.

subacute, and chronic clinical outcomes. This is viewed as an essential first step in the development and testing of clinical protocols and quality initiatives that may lessen the impact of these complications during cardiothoracic surgical recovery.

Why Is a New Label Needed?

Acute tamponade, subacute effusions, and chronic fibrosis around the heart and lungs have been described and studied for years as separate entities, usually ignoring their common root cause of retained blood. There is a growing body of biologic literature linking coagulation to inflammation and fibrosis coupled with a renewed focus on quality improvement that spurred interest in the study of RBS and its prevention.

There is overlap between RBS and postpericardiotomy syndrome (PPS), which was first described in the 1950s in patients after myocardial infarction and later in the 1960s after heart surgery.[5,6] A diagnosis of PPS rests on relatively nonspecific signs and symptoms of pleural and pericardial inflammation such as fever without alternative cause, pleuritic chest pain, friction rub, and evidence of new or worsening pleural or pericardial effusions (Table 1).[7,8] This diagnosis of PPS requires the presence of two of s findings and is demonstrated in 10% to 40% of patients after heart surgery.[9] This definition has limited utility because of its reliance on subjective clinical measures (eg, pleuritic chest pain) and lack of defined imaging criteria, as effusions are common to some degree in a majority of patients.[7] Initially, PPS was thought to be an autoimmune response, possibly triggered by a virus, whereby the patient develops antimyocardial antibodies against their own myocardial or pericardial cells.[10] Numerous prospective studies have been performed using potent drug regimens to broadly blunt the immune response, yet none has been uniformly successful in reducing PPS.[11–13] This further supports recent data suggesting that the inflammation associated with PPS is not mediated by an autoimmune process.[14,15]

TABLE 1. RBS Versus PPS

RBS (Based on the Presence of at Least One)	PPS (Based on the Presence of at Least Two)
Pleural effusion/hemothorax requiring drainage	Friction rub
Pericardial effusion requiring drainage	Fever without evidence of infection
Reexploration for washout of blood	Pleuritic chest pain
Interventions for postoperative pericardial constriction	Evidence of pleural effusions
Interventions for postoperative fibrothorax	Evidence of new or worsening pericardial effusion

RBS, retained blood syndrome; PPS, postpericardiotomy syndrome.

Although the old concept of PPS was useful description in the past, new scientific evidence suggests the need to refine the definition and to consider other hypothesis that may be more plausible and linked to potentially preventable root causes. We hypothesized that the root cause is retained blood and that the retained blood may ultimately drives an inflammatory response in the acute, subacute, and chronic setting that ensues. Working within this framework, strategies to prevent retained blood may help prevent these adverse outcomes.

Retained intrathoracic blood is common after cardiothoracic surgery and readily measured. Current data reveal the incidence of retained blood requiring removal by reopening the surgical incision and washout of the pericardial and pleural spaces, insertion of a new chest tube, or percutaneous pericardial or pleural drainage to be 13.8% to 22.7% (Table 2). In the last 30 years, there has been an exponential growth in our understanding of how coagulation leads directly to localized inflammation, both clinically after heart surgery and at the basic science level. Much has been learned about the natural history of ensuing localized and systemic inflammation that begins acutely and then transitions to subacute or chronic conditions, if unrelieved. A preponderance of data now leads us to suggest that this localized inflammatory response in the pleura and

TABLE 2. Reported Occurrence of Interventions for RBS After Heart Surgery

RBS	Incidence		Investigators
Acute interventions	253/6015	(4.2%)	Moulton et al[16]
	47/1188	(4.0%)	Christensen et al[1]
	566/18,891	(3.0%)	Vivacqua et al[17]
	148/2297	(6.4%)	Price et al[18]
Total		3.0%–6.4%	
Subacute pericardial	10/510	(2%)	Russo et al[19]
	117/5818	(2.0%)	Pompilio et al[20]
	260/21,416	(1.2%)	Ashikhmina et al[21]
Total		1.2%–2.0%	
Subacute pleural	12/202	(9.4%)	Lancey et al[22]
	41/345	(11.9%)	Payne et al[23]
Total		9.4%–11.9%	
Chronic		(0.2%–2.4%)	Gaudino et al[24]
Estimated RBS incidence		13.8%–22.7%	

RBS, retained blood syndrome.

pericardium is more likely caused by retained blood rather than by an antibody-mediated autoimmune response. To optimally prevent and treat these common conditions, a refined definition of the problem is needed, which considers the composite of these diagnoses, over the continuum of recovery, with a mutual root cause, which we believe is best labeled RBS. Ultimately, this updated definition will help investigators develop ways to study and prevent the constellation of complications related to retained blood.

Retained Blood Syndrome: Chronology and Definitions

Clinically, RBS can present on a spectrum over time. Thus, RBS can be subdivided further into acute RBS, subacute RBS, and chronic RBS (Fig. 2) Acute RBS is the most dramatic and is usually recognized in the first few hours after arrival in the ICU. Acute RBS manifests as high-volume blood accumulation with clot that requires washout. Subacute RBS presents close to or after discharge during early recovery, manifested as bloody and inflammatory effusions. Chronic RBS develops insidiously over months to years and is characterized by pericardial and pleural fibrosis. Along this spectrum, the common root cause may be inadequate evacuation of shed blood that may ultimately impact the local inflammatory state as well as the patient's physiologic recovery.

Acute RBS

Acute RBS is defined as clinically relevant retained blood requiring removal from the pericardial or pleural spaces in the first 24 to 48 hours after heart surgery. This can be objectively tracked by monitoring any invasive procedure needed to remove or wash out retained blood or blood clot via early reexploration. These objective and measureable interventions are specifically coded for and are included in The Society of Thoracic Surgeons

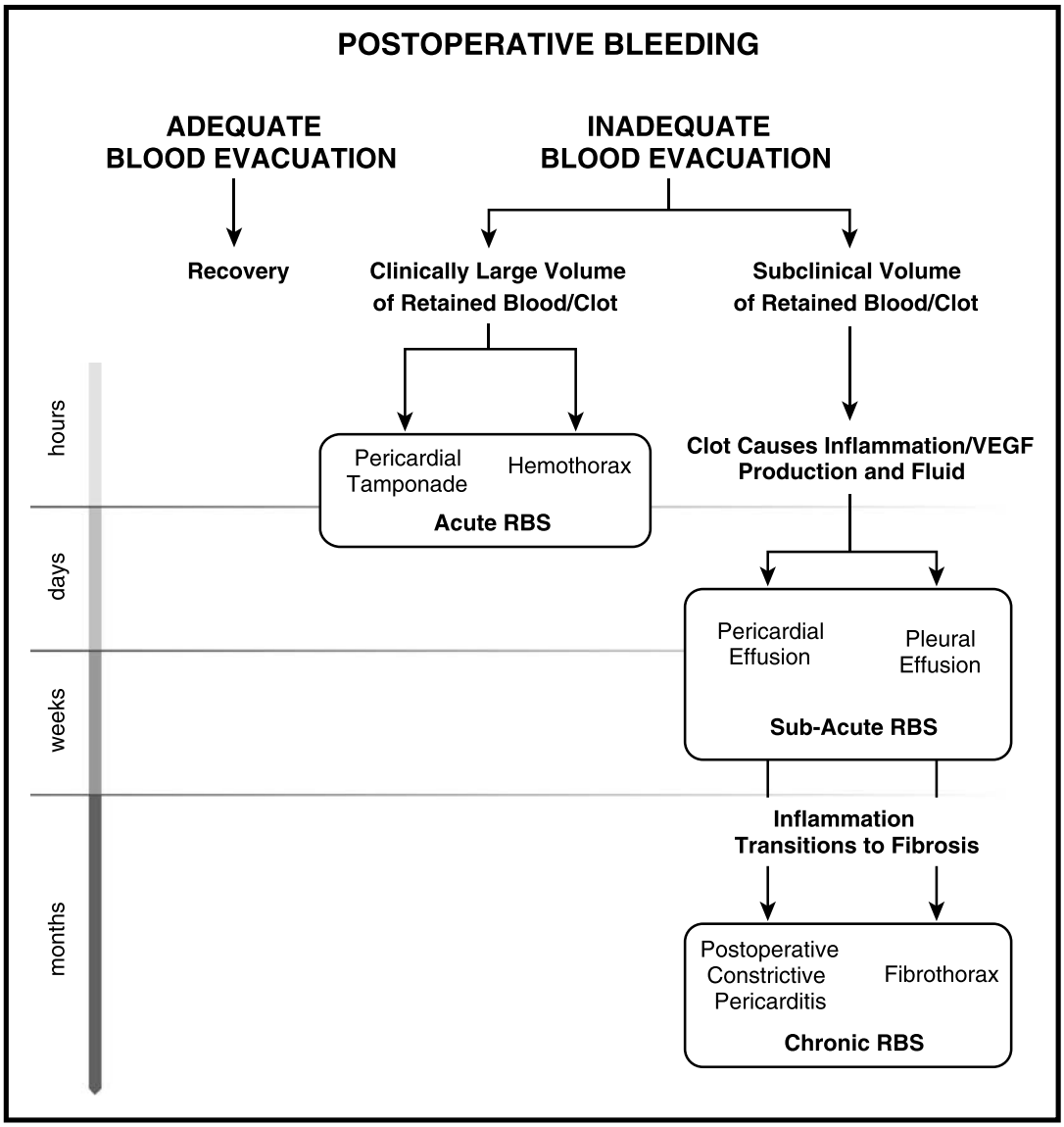

FIGURE 2. Incomplete evacuation of postsurgical blood causes RBS, which can cause acute, subacute, or chronic complications.

and other data registries. Based on these data, approximately 3% to 6% of patients currently require reexploration early after cardiac surgery, primarily for identification and repair of major surgical bleeding.[17,25–28] In 30% to 50% of reexplorations for mediastinal hemorrhage, no obvious bleeding source can be identified.[17,25] In these cases, the surgeon simply reopens and washes out retained blood and clot. This is a common finding for patients with coagulopathy, where the reexploration rates are considerably higher. The rationale for early surgical intervention is often tamponade because unevacuated shed blood clots outside the chest tubes and mechanically compresses the heart, lungs, and great vessels. It can be speculated that in some of these patients, reexploration could be avoided if adequate drainage of shed blood could be assured during correction of coagulopathy. Even patients with surgical sources of bleeding found on reexploration often have large mediastinal clot burden, again necessitating a washout of retained blood. Acute RBS can also present as a retained hemothorax early after heart surgery, which could potentially be cleared by adding an additional chest tube or again require reexploration to remove and wash out clot from around the lung. These procedures are also coded for and can easily be monitored with existing databases.

Subacute RBS

Subacute RBS is defined as the need for invasive interventions to drain bloody pericardial and pleural effusions in the weeks and months after heart surgery. This is objectively monitored by measuring how many patients need pericardiocentesis, pericardial window, thoracentesis, or a new chest tube for effusions after heart surgery. These effusions develop when smaller volumes of unevacuated blood around the heart and lungs accumulate without being drained, in the early hours after heart surgery. Our hypothesis is that an inflammatory process may develop, leading to effusions that worsen over the ensuing days or weeks. Persistent bloody fluid around the heart can be demonstrated in 60% to 85% of cardiac surgery patients.[29,30] Although most pericardial effusions are small, are subclinical, and resolve over time, 1.5% to 2% are large enough to require subsequent drainage.[20,21,30] Similarly, pleural fluid is a common finding in patients recovering from heart surgery, noted in nearly 42% to 91% of patients based on imaging studies.[31–33] The natural history for many of these effusions is to remain subclinical and resolve over time. At 1 month postoperatively, however, nearly 10% of cardiac surgery patients continue to have symptomatic bloody pleural effusions that occupy at least 25% of the hemithorax and require drainage.[34,35] Most patients typically require between one and three thoracenteses to evacuate these effusions, which[34,35] can persist beyond 1 month and lead to fibrothorax, with lung entrapment in severe cases.[36] Most pleural effusions occur on the left, particularly when the pleural space is opened to take down the internal mammary artery.[37,38] This suggests that fluid in the left chest can drain dependently from the pericardial and mediastinal spaces and chest wall.[32,39] Yet, even in the absence of a surgically opened pleural space, effusions often occur on the left, especially in the presence of a pericardial effusion. This suggests an association between pericardial inflammation and the development of pleural effusion in the absence of a pleurotomy.[31]

Chronic RBS

Chronic RBS is defined as the need to perform surgery to relieve the complications of fibrosis around the heart or lungs in the months or years after heart surgery. Currently, a definitive link between retained blood and chronic fibrosis has not been established; however, we hypothesize that such a link exists. The natural history of inflammatory effusions is that they either resolve or may continue on to a fibrotic response.[40,41] When examined closely for fibrotic constriction, patients with persistent effusions commonly demonstrate left chest pleural fibrosis.[31,41] Perhaps, the most well-known case is that of former US President Bill Clinton, who developed a well-publicized entrapped lung from fibrosis after a coronary artery bypass operation.[42] Although fibrothorax is more common, chronic fibrosis can also occur in the pericardial space as a result of chronic inflammation from retained blood. Gaudino et al[24] termed this phenomenon postoperative constrictive pericarditis and detailed a constellation of symptoms including dyspnea, a requirement for supplemental oxygen, and diminished exercise tolerance. In their review, they cited the impact of retained blood, subsequent pericardial effusion, and the association of resulting inflammatory cytokines and growth factors as contributing to this fibrosis, which was demonstrated in 0.2% to 2.4% of patients after heart surgery.

An objective measure of this outcome is the need for surgical treatment for fibrosis around the heart and lungs. Once fibrothorax or constrictive pericarditis occur, decortication and/or pericardiectomy may be required in an attempt to salvage physiologic end-organ function.[43] Although symptomatic relief can be dramatic for some, these procedures carry high morbidity and mortality, leading some to pursue medical therapy that has been shown to be relatively ineffective.

Pathophysiology of RBS

A modern understanding of the pathophysiology of acute, subacute, and chronic RBS links unevacuated blood to all of these conditions. For acute RBS, the pathophysiology is related to impaired physiology due to mechanical compression of the heart and lungs. For subacute and chronic RBS, an inflammatory condition may ensue as a direct result of the impact of coagulation on the mesothelial lining of the pericardium and pleura that drive the development of effusions and later fibrosis.

Acute RBS

The rate of bleeding and volume of shed blood that is unevacuated determine whether a patient presents with acute or subacute RBS. Dixon et al[44] demonstrated that the volume of chest drainage directly correlates with cardiac and respiratory decompensation postoperatively and found evidence suggesting a role for chest tube clogging in the development of acute RBS. They found that the greater the bleeding, the higher the risk of acute RBS with physiologic impairment due to mechanical compression of the heart or lungs. This explains why patients with acute RBS consistently have far worse outcomes; the mechanical compression of the heart and/or lungs leads to enough cardiopulmonary compromise to physiologically impair all organ systems, considerably increasing mortality and the length and complexity of recovery.[16,25] Although blood evacuation strategies

will not impact if a patient has surgical bleeding, they may allow the patient to be returned to the operating room with less physiologic compromise or avoid take-backs where surgical bleeding is not found. Thus, improving blood evacuation will not prevent surgical bleeding but may prevent RBS. Further studies are needed to determine if protocols that achieve more complete blood evacuation in bleeding patients will improve acute outcomes related to reduced acute RBS.

Subacute RBS

While it is tempting to speculate that postoperative pleural and pericardial effusions are related to heart failure, where transudative effusions predominate, heart failure alone does not seem to be a major contributing factor. In a majority of effusions seen after heart surgery, cytologic and chemical analysis reveals them to be bloody, inflammatory, and exudative, linking these to retained blood.[21,45]

Previous work attempted to link these PPS effusions to antimyocardial antibodies, suggesting an autoimmune etiology.[10,46] Growing evidence suggests that this is not a simple antibody response to incising the heart or pericardium.[14,15,47] With a more complete understanding of the inflammatory response that follows coagulation, a more plausible explanation is that once retained blood eventually clots within the pleural or pericardial spaces, thrombin and fibrin are generated. Both thrombin and fibrin are powerful chemoattractants of inflammatory cells that have been shown to drive a subacute localized inflammatory response by stimulating the mesothelial cells that line the pericardium and pleura to release inflammatory cytokines, possibly influenced by neutrophils and monocytes recruited to the site of inflammation.[48] Recently, Kramer et al[49] definitively demonstrated such an inflammatory intrapericardial response with increased concentrations of postoperative pericardial hemolized blood, oxidized hemoglobin, neutrophils, and monocytes from fluid from chest tubes in patients recovering from heart surgery. This shows that inflammatory responses capable of generating oxidative stress and subsequent cytokine-mediated inflammatory activation are present clinically in the pericardium, which might contribute to the local inflammation, which may contribute to the development of exudative effusions.[50,51]

One cytokine that may play a prominent role in this process of exudative effusion production is vascular endothelial growth factor (VEGF), a known permeability inducing agent.[52,53] Studies have shown high levels of VEGF receptors on mesothelial cells and elevated VEGF levels in exudative effusions.[53] Biologically, VEGFs are known to play a principal role in pleural and pericardial cellular permeability, leading to exudative effusions.[52] This occurs because mesothelial cells recruit inflammatory cells in a thrombin-mediated process that up-regulates VEGF production, leading to increased permeability, generating persistent effusions. Once stimulated by VEGF, mesothelial cells separate and leak serosanguinous fluid from the interstitial spaces into the pleural and pericardial spaces. This ongoing inflammatory reaction to clot may also provide an explanation for why exudative effusions often reaccumulate, even after several drainage procedures have been performed, contributing to delayed recovery and readmissions.[35,54] Further studies are needed to determine if limiting the amount of this retained blood can result in a reduction in clinically significant effusions after heart surgery.

Chronic RBS

Biologically, there is a well-described continuum between bleeding and clot-induced inflammation, leading to inflammatory, exudative bloody effusions in the subacute setting, and the subsequent development of late pleural or pericardial fibrosis chronically.[43,55] In contrast to the typical balance between fibrinolysis and coagulation in the pleural and pericardial spaces, some clinical, preclinical, and basic science studies suggest a disorder in fibrin turnover subsequent to a proinflammatory and procoagulant response, which is responsible for pleural and pericardial fibrosis.[55,56] When coagulation of retained blood occurs in these spaces, a fibrin neomatrix forms, creating the initial adhesions. Then, either a fibrinolytic response dominated by local tissue-type plasminogen activator clears the clot (leading to resolution) or an antifibrinolytic response dominated by plasminogen activator inhibitor prevents fibrinolysis, contributing to the subsequent fibrotic response.[43] It is possible that in some cases, a more pronounced procoagulant response, driven by retained blood, tips the scale toward fibrosis over fibrinolysis. It is feasible that this process leads to pleural and pericardial adhesions often found upon reoperation years later, thus increasing the difficulty, morbidity, and mortality seen with reoperative procedures. Although fibrosis may resolve over time, persistence can result in impaired long-term cardiac and respiratory dysfunction.[43] Further studies are needed to test the hypothesis that retained blood contributes to fibrosis in the pericardial or pleural spaces clinically in patients recovering from heart surgery.

Further studies are also needed to determine if limiting the amount of clot retained around the heart and lungs at the time of surgery will lessen the potential for long-term fibrotic complications in the pleural or pericardial spaces in the months and years after surgery.

RBS and Other Postoperative Complications

A growing body of literature suggests links between retained blood and the development of postoperative atrial fibrillation (POAF) and other complications. Postoperative atrial fibrillation is one of the most common complications after heart surgery, occurring in 20% to 60% of patients, and is a leading cause of hospital readmissions.[57] Patients with occluded chest tubes have been shown to have a higher rate of POAF.[4] In addition, several studies have demonstrated that more complete postoperative drainage of the pericardium reduces the incidence of POAF.[58,59] In a prospective study, Ege et al[60] demonstrated a reduction in POAF from 23.8% to 11.3% by using a redundant multidrainage tube strategy to reduce retained blood. In a similar study, Eryilmaz et al[61] reduced the incidence of POAF from 32.7% to 10.4% with a protocol aimed at minimizing retained pericardial blood early after operation. In all of these studies, there seems to be a link between pericardial effusion and development of POAF. Although the precise mechanism behind this effect is unclear, reduced inflammation from minimizing retained blood and clot in the pericardium may be contributory.

In addition, retained blood can impact the development of wound infections, although this link has not been studied

specifically after cardiac surgery. There is a clear association between retained blood and infection (empyema) in chest trauma patients,[62,63] where clot left behind has been shown to be a nidus for infection. Further outcome studies are warranted that will determine if limiting RBS reduces postoperative infections and other complications after cardiac surgery.

The link among RBS, POAF, and infections could be important in efforts to reduce hospital readmissions after heart surgery. The leading causes of 30-day readmissions currently include infection, POAF, and interventions for pleural and pericardial effusions, making this an attractive target for modern quality improvement strategies.[54,64,65]

Developing Strategies to Measure and Prevent RBS

Safe and effective drainage of postoperative blood and fluid after heart surgery requires a team approach to maximize evacuation of shed blood to assure ongoing drain patency. Surgeons insert chest drainage tubes in the operating room at the end of the case; nurses and critical care providers then monitor and manage chest tubes to maintain patency. They are expected to react promptly if chest tube obstruction is suspected, yet chest tube clogging is often invisible at the bedside until it has advanced to the point that physiological changes are evident.[4] Ensuring drain patency is certainly important but is a subject of current controversy because of a lack of study and because there are no set standards or guidelines.[66,67] In a best-practices publication by Day et al,[67] the authors examine current methods that are typically used at the bedside to prevent chest tube clogging, including chest tube stripping, milking, and tapping. They note a number of significant drawbacks and find that none has been shown to be uniformly effective. In dire clinical circumstances, tubes are opened at the bedside, and catheters are advanced in an attempt to clear clot.[68,69] The success of this maneuver is uncertain, and it may introduce risks of contamination and damage to intrathoracic structures. To date, clinicians lack any standardized method of chest tube management that has been shown to effectively maintain chest tube patency at the bedside.

There is evidence that maintaining chest tube patency with active clearance in the setting of bleeding can prevent intrathoracic blood accumulation and RBS.[70–72] This suggests the need for clinical studies to validate these findings and to determine the optimal clinical use protocols and best practices. Additional methods to reduce the degree of postoperative inflammation in the pleural and pericardial spaces may also be worthy of study.

Implications for Outcomes and Costs

When RBS is viewed as a composite of complications that occur in the acute, subacute, and chronic settings, specific intervention is required in roughly one in five patients recovering from surgery with potentially profound implications on patient recovery (Table 2). Today, a large number of cardiac surgical patients in the United States are discharged with a requirement for assistance, including home health or skilled nursing care.[73,74] Respiratory issues, weakness, deconditioning, and arrhythmias are cited as primary reasons for assistance after discharge and also lead to readmissions.[73,74] Many of these patients are returning for hospital readmissions. Government payers are reacting to these trends, and payment incentives are being proposed to discourage complications and readmissions.[75] In this new reimbursement model, the focus on quality is intertwined with payment that extends beyond the date of hospital discharge.[76] Cardiac surgery is an area of focus for these changes. If RBS can be prevented through adequate drainage early in recovery, this represents an important opportunity to improve patient outcomes that may have important financial implications.

Further Research

Recognizing the complications included in RBS and their common origin defines a potential target for clinical improvement and cost savings. Retained blood syndrome, as defined herein, is easily and objectively tracked. Baseline data regarding early complications exist in hospital coding and registry databases, using their existing definitions for these problems. Once a baseline has been established, regression analysis can be performed to determine if RBS is an independent risk factor for poor outcomes or simply associated with worse comorbidities. In addition, research is needed to develop chest tube patency protocols and study how it is best maintained and determine if more complete evacuation of blood can indeed reduce the incidence of RBS. Additional blood evacuation strategies, such as the location and number of drainage tubes and timing of removal, are also of interest with regard to RBS and other outcomes. This will take a team effort from surgeons, operating room and ICU personnel, and many others who participate in the patient's early recovery after heart surgery. Randomized clinical trials that pursue evidence-based guidelines for optimal chest drainage protocols will eventually be feasible to minimize RBS.

CONCLUSIONS

Advances in our understanding of the biologic impact of retained intrathoracic blood and its relationship to inflammation and fibrosis suggest the need to recognize a constellation of related complications that we term RBS. Retained blood syndrome impacts approximately one in five cardiac surgery patients, making this a sizable population to target for quality improvement. Although further scientific and clinical evidence is necessary to validate this proposed classification, RBS is biologically plausible and is linked to objectively measurable outcomes. Further study is clearly needed to validate the incidence and consequences of RBS in large cardiac surgical databases as well as to determine if this is in fact an independent risk factor for poor outcomes. Additional study on the biologic front is needed to continue to dissect the etiologic factors that contribute to these complications and to determine if retained blood is indeed the perpetrator, as we propose, or a bystander. Finally, we must test the hypothesis that better postoperative drainage strategies will reduce the incidence of RBS, improve outcomes, and reduce costs.

REFERENCES

1. Christensen MC, Dziewior F, Kempel A, von Heymann C. Increased chest tube drainage is independently associated with adverse outcome after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2012;26:46–51.
2. Wynne R, Botti M, Copley D, Bailey M. The normative distribution of chest tube drainage volume after coronary artery bypass grafting. *Heart Lung*. 2007;36:35–42.
3. Shalli S, Saeed D, Fukamachi K, et al. Chest tube selection in cardiac and thoracic surgery: a survey of chest tube–related complications and their management. *J Card Surg*. 2009;24:503–509.

4. Karimov JH, Gillinov AM, Schenck L, et al. Incidence of chest tube clogging after cardiac surgery: a single-center prospective observational study. *Eur J Cardiothorac Surg*. 2013;44:1029–1036.
5. Dressler W. A post-myocardial infarction syndrome; preliminary report of a complication resembling idiopathic, recurrent, benign pericarditis. *J Am Med Assoc*. 1956;160:1379–1383.
6. Schramel R, Williamson W Jr, Iglesias F, Creech O Jr. Post-pericardiotomy syndrome: observations regarding auto-immune mechanisms in its etiology. *Surg Forum*. 1961;12:239–241.
7. Imazio M, Brucato A, Ferrazzi P, Spodick DH, Adler Y. Postpericardiotomy syndrome: a proposal for diagnostic criteria. *J Cardiovasc Med (Hagerstown)*. 2013;14:351–353.
8. Imazio M, Brucato A, Rovere ME, et al. Contemporary features, risk factors, and prognosis of the post-pericardiotomy syndrome. *Am J Cardiol*. 2012;108:1183–1187.
9. Imazio M. The post-pericardiotomy syndrome. *Curr Opin Pulm Med*. 2012;18:366–374.
10. De Scheerder I, Wulfrank D, Van Renterghem L, et al. Association of anti-heart antibodies and circulating immune complexes in the post-pericardiotomy syndrome. *Clin Exp Immunol*. 1984;57:423–428.
11. Imazio M, Brucato A, Ferrazzi P, et al. Colchicine for prevention of post-pericardiotomy syndrome and postoperative atrial fibrillation: the COPPS-2 randomized clinical trial. *JAMA*. 2014;312:1016–1023.
12. Bunge JJ, van Osch D, Dieleman JM, et al. Dexamethasone for the prevention of postpericardiotomy syndrome: a DExamethasone for Cardiac Surgery substudy. *Am Heart J*. 2014;168:126–131 e121.
13. Imazio M, Brucato A, Markel G, et al. Meta-analysis of randomized trials focusing on prevention of the postpericardiotomy syndrome. *Am J Cardiol*. 2011;108:575–579.
14. Hoffman M, Fried M, Jabareen F, et al. Anti-heart antibodies in post-pericardiotomy syndrome: cause or epiphenomenon? A prospective, longitudinal pilot study. *Autoimmunity*. 2012;35:241–245.
15. Akl ES, Latif N, Dunn MJ, Rose ML, Yacoub MH. Antiheart antibodies following open heart surgery: incidence and correlation with postpericardiotomy syndrome. *Eur J Cardiothorac Surg*. 1992;6:503–507.
16. Moulton MJ, Creswell LL, Mackey ME, Cox JL, Rosenbloom M. Reexploration for bleeding is a risk factor for adverse outcomes after cardiac operations. *J Thorac Cardiovasc Surg*. 1996;111:1037–1046.
17. Vivacqua A, Koch CG, Yousuf AM, et al. Morbidity of bleeding after cardiac surgery: is it blood transfusion, reoperation for bleeding, or both? *Ann Thorac Surg*. 2011;91:1780–1790.
18. Price S, Prout J, Jaggar SI, Gibson DG, Pepper JR. 'Tamponade' following cardiac surgery: terminology and echocardiography may both mislead. *Eur J Cardiothorac Surg*. 2004;26:1156–1160.
19. Russo AM, O'Connor WH, Waxman HL. Atypical presentations and echocardiographic findings in patients with cardiac tamponade occurring early and late after cardiac surgery. *Chest*. 1993;104:71–78.
20. Pompilio G, Filippini S, Agrifoglio M, et al. Determinants of pericardial drainage for cardiac tamponade following cardiac surgery. *Eur J Cardiothorac Surg*. 2011;39:e107–e113.
21. Ashikhmina EA, Schaff HV, Sinak LJ, et al. Pericardial effusion after cardiac surgery: risk factors, patient profiles, and contemporary management. *Ann Thorac Surg*. 2010;89:112–118.
22. Lancey RA, Gaca C, Vander Salm TJ. The use of smaller, more flexible chest drains following open heart surgery: an initial evaluation. *Chest*. 2001; 119:19–24.
23. Payne M, Magovern GJ Jr, Benckart DH, et al. Left pleural effusion after coronary artery bypass decreases with a supplemental pleural drain. *Ann Thorac Surg*. 2002;73:149–152.
24. Gaudino M, Anselmi A, Pavone N, Massetti M. Constrictive pericarditis after cardiac surgery. *Ann Thorac Surg*. 2013;95:731–736.
25. Hall TS, Brevetti GR, Skoultchi AJ, Gregory P, Spotnitz AJ. Re-exploration for hemorrhage following open heart surgery differentiation on the causes of bleeding and the impact on patient outcomes. *Ann Thorac Cardiovasc Surg*. 2001;7:352–357.
26. Karthik S, Grayson AD, McCarron EE, Pullan DM, Desmond MJ. Reexploration for bleeding after coronary artery bypass surgery: risk factors, outcomes, and the effect of time delay. *Ann Thorac Surg*. 2004; 78:527–534.
27. Mehta RH, Sheng S, O'Brien SM, et al. Reoperation for bleeding in patients undergoing coronary artery bypass surgery: incidence, risk factors, time trends, and outcomes. *Circ Cardiovasc Qual Outcomes*. 2009;2:583–590.
28. Vuylsteke A, Pagel C, Gerrard C, et al. The Papworth Bleeding Risk Score: a stratification scheme for identifying cardiac surgery patients at risk of excessive early postoperative bleeding. *Eur J Cardiothorac Surg*. 2011;39: 924–930.
29. Schleder S, Dittmar M, Poschenrieder F, et al. Diagnosis of pericardial effusion with a new generation hand-carried ultrasound device in cardiothoracic intensive care unit patients. *Acta Radiol*. 2012;53:1133–1136.
30. Pepi M, Muratori M, Barbier P, et al. Pericardial effusion after cardiac surgery: incidence, site, size, and haemodynamic consequences. *Br Heart J*. 1994;72:327–331.
31. Peng MJ, Vargas FS, Cukier A, et al. Postoperative pleural changes after coronary revascularization. Comparison between saphenous vein and internal mammary artery grafting. *Chest*. 1992;101:327–330.
32. Vargas FS, Cukier A, Hueb W, Teixeira LR, Light RW. Relationship between pleural effusion and pericardial involvement after myocardial revascularization. *Chest*. 1994;105:1748–1752.
33. Landymore RW, Howell F. Pulmonary complications following myocardial revascularization with the internal mammary artery graft. *Eur J Cardiothorac Surg*. 1990;4:156–161.
34. Light RW. Pleural effusions following cardiac injury and coronary artery bypass graft surgery. *Semin Respir Crit Care Med*. 2001;22:657–664.
35. Light RW, Rogers JT, Moyers JP, et al. Prevalence and clinical course of pleural effusions at 30 days after coronary artery and cardiac surgery. *Am J Respir Crit Care Med*. 2002;166(12 pt 1):1567–1571.
36. Peng MC, Hou CJ, Li JY, Hu PY, Chen CY. Prevalence of symptomatic large pleural effusions first diagnosed more than 30 days after coronary artery bypass graft surgery. *Respirology*. 2007;12:122–126.
37. Iyem H, Islamoglu F, Yagdi T, et al. Effects of pleurotomy on respiratory sequelae after internal mammary artery harvesting. *Tex Heart Inst J*. 2006;33: 116–121.
38. Hurlbut D, Myers ML, Lefcoe M, Goldbach M. Pleuropulmonary morbidity: internal thoracic artery versus saphenous vein graft. *Ann Thorac Surg*. 1990;50:959–964.
39. Wheatcroft M, Shrivastava V, Nyawo B, Rostron A, Dunning J. Does pleurotomy during internal mammary artery harvest increase post-operative pulmonary complications? *Interact Cardiovasc Thorac Surg*. 2005;4: 143–146.
40. Lee YC, Vaz MA, Ely KA, et al. Symptomatic persistent post-coronary artery bypass graft pleural effusions requiring operative treatment: clinical and histologic features. *Chest*. 2001;119:795–800.
41. Charniot JC, Zerhouni K, Kambouchner M, et al. Persistent symptomatic pleural effusion following coronary bypass surgery: clinical and histologic features, and treatment. *Heart Vessels*. 2007;22:16–20.
42. Altman L. Clinton's 4-Hour Surgery Went Well, Doctors Say. *New York Times*. March 11, 2005. Website: http://www.nytimes.com/2005/03/11/us/clintons-4hour-surgery-went-well-doctors-say.html?_r=0. Accessed October 2015.
43. Jantz MA, Antony VB. Pleural fibrosis. *Clin Chest Med*. 2006;27:181–191.
44. Dixon B, Santamaria JD, Reid D, et al. The association of blood transfusion with mortality after cardiac surgery: cause or confounding? *Transfusion*. 2013;53:19–27.
45. Sadikot RT, Rogers JT, Cheng DS, Moyers P, Rodriguez M, Light RW. Pleural fluid characteristics of patients with symptomatic pleural effusion after coronary artery bypass graft surgery. *Arch Intern Med*. 2000;160: 2665–2668.
46. Engle MA, McCabe JC, Ebert PA, Zabriskie J. The Postpericardiotomy syndrome and antiheart antibodies. *Circulation*. 1974;49:401–406.
47. Bartels C, Honig R, Burger G, Diehl V, de Vivie R. The significance of anticardiolipin antibodies and anti-heart muscle antibodies for the diagnosis of postpericardiotomy syndrome. *Eur Heart J*. 1994;15:1494–1499.
48. Szaba FM, Smiley ST. Roles for thrombin and fibrin(ogen) in cytokine/chemokine production and macrophage adhesion in vivo. *Blood*. 2012;99: 1053–1059.
49. Kramer PA, Chacko BK, Ravi S, et al. Hemoglobin-associated oxidative stress in the pericardial compartment of postoperative cardiac surgery patients. *Lab Invest*. 2015;95:132–141.

50. Light RW. Cytokines and the pleura. In: Light RW, ed. *Pleural Diseases*. Philadelphia, PA USA: Lippincott Williams and Wilkins; 2007:44–54.
51. Mandl-Weber S, Cohen CD, Haslinger B, Kretzler M, Sitter T. Vascular endothelial growth factor production and regulation in human peritoneal mesothelial cells. *Kidney Int*. 2007;61:570–578.
52. Grove CS, Lee YC. Vascular endothelial growth factor: the key mediator in pleural effusion formation. *Curr Opin Pulm Med*. 2002;8:294–301.
53. Thickett DR, Armstrong L, Millar AB. Vascular endothelial growth factor (VEGF) in inflammatory and malignant pleural effusions. *Thorax*. 1999;54: 707–710.
54. Magnus PC, Kramer RS, Ross CS, et al. Abstract 13474: causes of 30-day readmission after cardiac surgery in Northern New England. *Circulation*. 2011;124:A13474.
55. Shetty SJ, Idell S. Pleural fibrosis. In: Light RW, LEE YC, eds. *Textbook of Pleural Diseases*. Boca Raton, FL USA: CRC Press; 2008:101–112.
56. Idell S, Girard W, Koenig KB, McLarty J, Fair DS. Abnormalities of pathways of fibrin turnover in the human pleural space. *Am Rev Respir Dis*. 1991;144:187–194.
57. LaPar DJ, Speir AM, Crosby IK, et al. Postoperative atrial fibrillation significantly increases mortality, hospital readmission, and hospital costs. *Ann Thorac Surg*. 2014;98:527–533.
58. Arsenault KA, Yusuf AM, Crystal E, et al. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. *Cochrane Database Syst Rev.* 2013;1:CD003611.
59. Biancari F, Mahar MA. Meta-analysis of randomized trials on the efficacy of posterior pericardiotomy in preventing atrial fibrillation after coronary artery bypass surgery. *J Thorac Cardiovasc Surg*. 2010;139:1158–1161.
60. Ege T, Tatli E, Canbaz S, et al. The importance of intrapericardial drain selection in cardiac surgery. *Chest*. 2004;126:1559–1562.
61. Eryilmaz S, Emiroglu O, Eyileten Z, et al. Effect of posterior pericardial drainage on the incidence of pericardial effusion after ascending aortic surgery. *J Thorac Cardiovasc Surg*. 2006;132:27–31.
62. DuBose J, Inaba K, Demetriades D, et al. Management of post-traumatic retained hemothorax: a prospective, observational, multicenter AAST study. *J Trauma Acute Care Surg*. 2012;72:11–22.
63. DuBose J, Inaba K, Okoye O, et al. Development of posttraumatic empyema in patients with retained hemothorax: results of a prospective, observational AAST study. *J Trauma Acute Care Surg*. 2012;73:752–757.
64. Maniar HS, Bell JM, Moon MR, et al. Prospective evaluation of patients readmitted after cardiac surgery: analysis of outcomes and identification of risk factors. *J Thorac Cardiovasc Surg*. 2014;147:1013–1018.
65. Iribarne A, Chang H, Alexander JH, et al. Readmissions after cardiac surgery: experience of the National Institutes of Health/Canadian Institutes of Health research cardiothoracic surgical trials network. *Ann Thorac Surg*. 2014;98:1274–1280.
66. Halm MA. To strip or not to strip? Physiological effects of chest tube manipulation. *Am J Crit Care*. 2007;16:609–612.
67. Day TG, Perring RR, Gofton K. Is manipulation of mediastinal chest drains useful or harmful after cardiac surgery? *Interact Cardiovasc Thorac Surg*. 2008;7:888–890.
68. Boyacioglu K, Kalender M, Ozkaynak B, Mert B, Kayalar N, Erentuğ V. A new use of Fogarty catheter: chest tube clearance. *Heart Lung Circ*. 2014;23:e229–e230.
69. Halejian BA, Badach MJ, Trilles F. Maintaining chest tube patency. *Surg Gynecol Obstet*. 1988;167:521.
70. Arakawa Y, Shiose A, Takaseya T, et al. Superior chest drainage with an active tube clearance system: evaluation of a downsized chest tube. *Ann Thorac Surg*. 2011;91:580–583.
71. Perrault LP, Pellerin M, Carrier M, et al. The PleuraFlow Active Chest Tube Clearance System: initial clinical experience in adult cardiac surgery. *Innovations*. 2012;7:354–358.
72. Shalli S, Boyle EM, Saeed D, et al. The active tube clearance system: a novel bedside chest-tube clearance device. *Innovations*. 2010;5:42–47.
73. Carey JS, Parker JP, Robertson JM, Misbach GA, Fisher AL. Hospital discharge to other healthcare facilities: impact on in-hospital mortality. *J Am Coll Surg*. 2003;197:806–812.
74. Lazar HL, Fitzgerald CA, Ahmad T, et al. Early discharge after coronary artery bypass graft surgery: are patients really going home earlier? *J Thorac Cardiovasc Surg*. 2001;121:943–950.
75. Berenson RA, Paulus RA, Kalman NS. Medicare's readmissions-reduction program—a positive alternative. *N Engl J Med*. 2012;366: 1364–1366.
76. Clancy CM. New hospital readmission policy links financial and quality incentives. *J Nurs Care Qual*. 2013;28:1–4.

