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Airway Hemorrhage Complicating Pulmonary Thromboendarterectomy: Risk Factors and Outcomes

Alisha A. Kabadi, MD,[1] Timothy M. Fernandes, MD,[1] Demosthenes G. Papamatheakis, MD,[1] David S. Poch, MD,[1] Nick H. Kim, MD,[1] Jenny Z. Yang, MD,[1] Angela Bautista, MS,[1] Victor G. Pretorius, MBchB,[2] Michael M. Madani, MD,[2,*] and Kim M. Kerr, MD[1,*]

ABSTRACT

BACKGROUND Airway hemorrhage is a known complication of pulmonary thromboendarterectomy (PTE) in patients with chronic thromboembolic pulmonary hypertension. Predisposing factors for postoperative airway hemorrhage have not been well described. The aims of this study were to determine the incidence and outcomes of airway hemorrhage after PTE and to identify potential risk factors.

METHODS This was a retrospective chart review of subjects undergoing PTE between 2015 and 2019. Postoperative airway hemorrhage was defined as significant endobronchial bleeding requiring withholding anticoagulation, bronchial blocker placement, and/or extracorporeal membrane oxygenation (ECMO).

RESULTS Of 877 subjects who underwent PTE, 58 subjects (6.6%) developed postoperative airway hemorrhage. Subjects with hemorrhage were more likely to be women (60% vs 45%, $P = .03$), to be older (57.8 vs 54.0 years, $P = .04$), and to have a higher incidence of preoperative hemoptysis (19.0% vs 7.6%, $P = .006$) compared with control subjects (subjects without airway hemorrhage). Those with hemorrhage had significantly higher preoperative right atrial pressure ($P = .002$) and pulmonary vascular resistance ($P < .001$) and a higher incidence of residual pulmonary hypertension ($P = .005$). Airway hemorrhage management included ECMO with bronchial blocker (n = 2), bronchial blocker without ECMO (n = 26), or withholding anticoagulation alone until bleeding subsided (n = 30). Mortality was significantly higher in those with airway hemorrhage compared with control subjects (13.8% vs 1.2%, $P < .001$).

CONCLUSIONS The incidence of postoperative airway hemorrhage is low but associated with significant mortality. Older age, female sex, preoperative hemoptysis, and worse preoperative pulmonary hypertension were associated with an increased risk of developing postoperative airway hemorrhage.

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Pulmonary thromboendarterectomy (PTE) is the recommended intervention for patients with chronic thromboembolic pulmonary hypertension (CTEPH) who are deemed to be operative candidates. PTE has been demonstrated to improve pulmonary hemodynamics and long-term survival.[1-3] Although operative mortality has fallen below 5% at expert centers, complications including reperfusion pulmonary edema and persistent pulmonary hypertension can occur and contribute to postoperative mortality.[4,5]

Airway hemorrhage is a rare complication of PTE, for which the etiology and potential predisposing factors are not clearly delineated. Several mechanisms have been hypothesized including surgical trauma during complex dissections, friability of endarterectomized vessels, increased capillary permeability from restored perfusion, and bleeding from systemic-pulmonary collateral arteries.[6-8] Previous series have reported an incidence of

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*Drs Madani and Kerr are co-senior authors.

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[1]Division of Pulmonary, Critical Care & Sleep Medicine, University of California San Diego, La Jolla, California; and [2]Division of Cardiovascular and Thoracic Surgery, University of California San Diego, La Jolla, California

Address correspondence to Dr Kabadi, Division of Pulmonary, Critical Care & Sleep Medicine, 9300 Campus Point Dr, MC 7381, La Jolla, CA 92037; email: aakabadi@health.ucsd.edu.

post-PTE airway hemorrhage of 0.5% to 5% with an associated mortality rate of 50% to 70%.[6,9-12]

In this study we determined the incidence of postoperative airway hemorrhage in 877 patients with CTEPH or symptomatic chronic thromboembolic disease without resting pulmonary hypertension who underwent PTE at University of California, San Diego (UCSD) between 2015 and 2019. Preoperative characteristics and postoperative course of patients with airway hemorrhage after PTE are described, and potential predisposing risk factors were identified.

PATIENTS AND METHODS

This is a retrospective study of all UCSD PTE patients entered into an Institutional Review Board-approved quality improvement database between January 2015 and December 2019. Eight hundred eighty-four patients underwent PTE performed by 1 of 2 surgeons (M.M.M. or V.G.P.). Seven subjects were excluded from the analysis because they were found to have a diagnosis other than CTEPH during surgery (Figure 1). This study, conducted using this quality improvement database, was granted an exemption from the UCSD Institutional Review Board.

Fifty-eight subjects with postoperative airway hemorrhage occurring intraoperatively or at any point during the postoperative course were identified. Airway hemorrhage was defined as bleeding requiring a change in standard postoperative management, such as withholding anticoagulation alone or bronchial blocker placement with or without extracorporeal membrane oxygenation (ECMO) support. Withholding anticoagulation was defined as a delay of >12 hours in initiating postoperative anticoagulation or the temporary postoperative cessation of anticoagulation due to airway hemorrhage. Those with airway hemorrhage were further subdivided into 2 groups reflecting the severity of hemorrhage: minor (withholding anticoagulation alone) and massive (withholding anticoagulation and bronchial blocker placement, with or without ECMO). The remaining 819 subjects without airway hemorrhage were identified as control subjects (Figure 1).

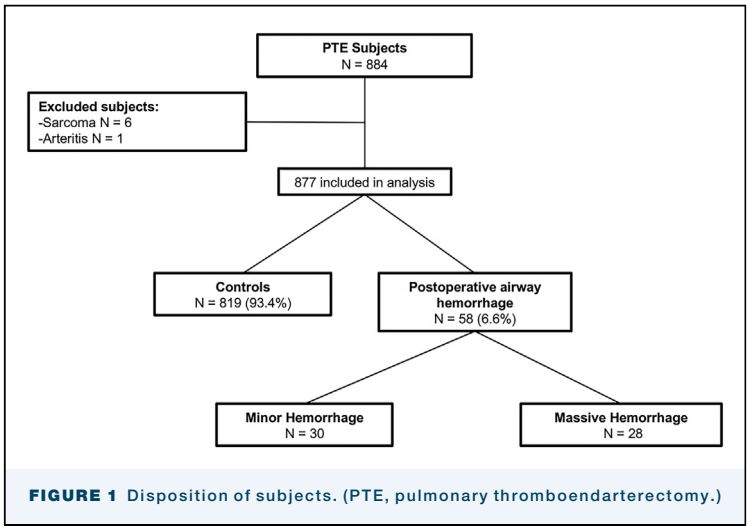

FIGURE 1 Disposition of subjects. (PTE, pulmonary thromboendarterectomy.)

Data on demographics, preoperative comorbidities, medical therapy, hemodynamics, intraoperative findings, airway hemorrhage characteristics and management, and postoperative course were collected. A history of preoperative hemoptysis was defined as 1 or more occurrences of hemoptysis at any point before surgery that met at least 1 of the following criteria: volume > 100 mL (one-half cup), required withholding chronic anticoagulation, and/or required hospital admission for evaluation.

Preoperative hemodynamics were obtained from the right heart catheterization performed closest to the time of PTE. Postoperative hemodynamics were reported using with values obtained immediately before removal of the pulmonary artery catheter in the intensive care unit (ICU). Postoperative pulmonary vascular resistance (PVR) was estimated by substituting central venous pressure for pulmonary artery wedge pressure, because pulmonary artery wedge pressure cannot be measured postoperatively. Residual postoperative pulmonary hypertension was defined as PVR > 400 dyn·s/cm^5.

The location of chronic thromboembolic disease (proximal vs distal) was defined by the intraoperative UCSD level classification system.[13] Proximal disease was defined as UCSD level 1 or 2 (disease starting in the main, descending, or lobar pulmonary artery) in either or both lungs, and distal disease was defined as UCSD level 3 or 4 (disease starting in the segmental or subsegmental artery) in both lungs.

The duration of mechanical ventilation was assessed as the number of days free of respiratory support within 28 days of surgery (ventilator-free days), calculated as 28 minus the number of days on mechanical ventilation. ICU and hospital-free days were calculated similarly. Subjects with number of days > 28 and subjects who died during their hospital course received a score of 0.

Data were analyzed by comparing the postoperative airway hemorrhage group with the control group. Further analysis compared minor and massive hemorrhage groups with each other and with control subjects. Statistical analysis was performed using GraphPad Prism statistical software. Continuous variables that were normally distributed are expressed as mean ± SD; hemodynamics and lengths of stay are presented as median with interquartile ranges. We used the Student's *t* test to compare means and the Mann-Whitney test to compare medians. Categorical variables were expressed

as absolutes with percentages and analyzed using Fisher's exact or χ^2 tests. $P \leq .05$ was considered statistically significant. Using SPSS statistical software version 28 (SPSS IBM), univariate and multivariate logistic regression analyses were performed to calculate odds ratio (OR) and 95% CI for continuous and categorical variables that significantly deferred between the airway hemorrhage and control groups.

RESULTS

Of 877 PTE subjects included in this study, 6.6% of them (58) had an incidence of postoperative airway hemorrhage. The postoperative airway hemorrhage subjects were older with a higher percentage of women (60% vs 45%, $P = .03$) compared with control subjects. A history of preoperative hemoptysis was significantly higher in those with airway hemorrhage vs control subjects (19.0% vs 7.6%, $P = .006$). There was a significantly higher preoperative New York Heart Association functional class in the airway hemorrhage group compared with control subjects but no difference in prevalence of deep vein thrombosis, underlying thrombophilia, diabetes, prior malignancy, or splenectomy between groups (Table 1). Multivariate analysis identified advanced age (OR, 1.022), female gender (OR, 2.141), history of preoperative hemoptysis (OR, 3.048), and a higher preoperative PVR (OR, 1.001) to be significantly associated with airway hemorrhage (Table 2).

Most subjects in both groups were on pulmonary hypertension-targeted therapy before surgery, with a nonsignificant trend toward more therapy used in the airway hemorrhage group (Supplemental Table 1). There was no difference in use of riociguat or parenteral prostacyclin between groups. Preoperative hemodynamics were significantly worse in the airway hemorrhage group vs control subjects, with higher right atrial pressures, mean pulmonary artery pressures, PVR, and total pulmonary resistance, combined with a lower cardiac index (Table 3).

Analysis of the international normalized ratio and platelet count drawn 1 day before surgery in those with airway hemorrhage revealed 5 subjects with an international normalized ratio between 1.5 and 1.9 and 2 subjects with an international normalized ratio > 2.0 (reversed in the operating room with prothrombin complex concentrate). Three subjects had a platelet count of 50,000 to 100,000 and 1 subject had a platelet count < 50,000.

Intraoperative clot location was more likely to be classified as distal disease in the airway hemorrhage group vs control subjects (38% vs 27%, $P = .09$). Ventilator-free days, ICU-free days, and hospital-free days were all significantly lower in the airway hemorrhage group. The airway hemorrhage group had worse postoperative hemodynamics including significantly higher mean pulmonary artery pressures, PVR, and total pulmonary resistance; lower cardiac output; and a higher incidence of residual pulmonary hypertension. ECMO was used more frequently among subjects with airway hemorrhage (Tables 3 and 4).

The characteristics and treatment of airway hemorrhage are listed in Supplemental Table 2. Forty-two subjects (71%) developed airway hemorrhage intraoperatively or on postoperative day 0, with 12 occurring on postoperative day 1 and 14 occurring later. Airway hemorrhage was localized to the right lung in 21 subjects, the left lung in 27 subjects, and bilateral in 2 subjects. Hemorrhage was localized to a single lobe in 48 subjects, with most occurring in the lower lobes. Full-thickness pulmonary artery vessel disruption occurred in 5 subjects; 4 subjects were treated with a mixed biologic glue and oxidized cellulose-based hemostatic agent and 1 subject with vessel ligation. Seven subjects had perioperative bleeding at other sites (mediastinal bleeding in 6 and incisional site bleeding in 1).

Thirty subjects were managed by withholding anticoagulation alone (minor hemorrhage) for a median of

TABLE 1 Preoperative Characteristics

Characteristics	Control Subjects (n = 819)	Postoperative Airway Hemorrhage Subjects (n = 58)	P
Age, y	54.0 ± 15.5	57.8 ± 15.0	.04[a]
Female sex	367 (45)	35 (60)	.03[a]
New York Heart Association functional classes I/II/III/VI, %	1/21/71/6	0/7/84/9	.04[a]
Prior deep vein thrombosis	515 (63)	37 (64)	>.99
Known thrombophilia	207 (25)	16 (28)	.76
History of malignancy	90 (11)	3 (5)	.19
Diabetes	98 (12)	10 (17)	.22
History of splenectomy	30 (4)	2 (3)	>.99
History of preoperative hemoptysis	62 (7.6)	11 (19.0)	.006[a]

[a]Statistically significant $P \leq .05$. Values are mean ± SD or n (%) unless otherwise defined.

TABLE 2 Logistic Regression Analysis (Risk Factors for Airway Hemorrhage)

	Univariate		Multivariate	
Risk Factor	Odds Ratio	95% CI	Odds Ratio	95% CI
Advanced age (per 1 y)	1.016	0.998-1.035	1.022[a]	1.003-1.041
Female sex	1.929[a]	1.123-3.313	2.141[a]	1.223-3.749
History of deep vein thrombosis	1.070	0.617-1.858		
History of preoperative hemoptysis	2.794[a]	1.381-5.652	3.058[a]	1.459-6.408
Use of preoperative pulmonary hypertension meds	1.651	0.946-2.879		
Preoperative right atrial pressure	1.042[a]	1.007-1079		
Preoperative pulmonary vascular resistance (per 1 dyn·s/cm^{-5})	1.001[a]	1.000-1.002	1.001[a]	1.000-1.002
Distal disease	1.726[a]	1.000-2.978		

[a]Statistically significant $P \leq .05$.

TABLE 3 Preoperative and Postoperative Hemodynamics

Hemodynamics	Control Subjects (n = 819)	Postoperative Airway Hemorrhage Subjects (n = 58)	P
Right atrial pressure, mm Hg			
Preoperative	9.0 [6.0, 12.0]	11.0 [7.0, 15.0]	.002[a]
Postoperative	8.0 [6.0, 10.0]	8.0 [6.0, 11.0]	.28
Mean pulmonary artery pressure, mm Hg			
Preoperative	42.0 [32.0, 49.0]	46.0 [36.5, 52.0]	.01[a]
Postoperative	22.0 [18.0, 26.0]	26.0 [22.5, 31.0]	<.001[a]
Pulmonary artery wedge pressure, mm Hg			
Preoperative	12.0 [9.0, 14.3]	12.0 [8.0, 15.0]	.58
Postoperative	N/A	N/A	
Cardiac output, L/min			
Preoperative	4.7 [3.8, 5.7]	3.8 [3.2, 4.9]	<.001[a]
Postoperative	5.6 [4.9, 6.5]	5.3 [4.6, 5.9]	.05[a]
Cardiac index, L/min/m^2			
Preoperative	2.3 [1.9, 2.7]	2.0 [1.7, 2.5]	<.001[a]
Postoperative	2.7 [2.4, 3.1]	2.6 [2.4, 3.1]	.31
Pulmonary vascular resistance, dyn·s/cm^{-5}			
Preoperative	499 [304, 736]	709 [433, 1026]	<.001[a]
Postoperative	196 [145, 267]	275 [210, 390]	<.001[a]
Total pulmonary resistance, dyn·s/cm^{-5}			
Preoperative	692 [477, 951]	911 [590, 1244]	<.001[a]
Postoperative	317 [245, 393]	402 [305, 498]	<.001[a]

[a]Statistically significant $P \leq .05$. Values are median [Q1, Q3]. N/A, not applicable.

1.0 days (range, 0.5-15). The massive hemorrhage group comprised 28 subjects (3.2% of the total study population) and were managed by withholding anticoagulation (median, 2.0 days; range, 0.5-10) and bronchial blocker placement in the operating room. Six subjects with massive hemorrhage required ECMO. Indications for ECMO were airway hemorrhage (n = 2) and severe reperfusion edema with cardiogenic shock (n = 4).

A comparison of the minor and massive hemorrhage groups found a significantly higher percentage of female subjects in the massive hemorrhage group but no differences in the other previously defined significant risk factors. Airway hemorrhage occurred intraoperatively or postoperative on day 0 in all subjects with massive hemorrhage compared with only 45% of subjects with minor hemorrhage. The median duration of withholding anticoagulation was longer in the massive hemorrhage group, with significantly more subjects requiring blood products. Ventilator-free days and ICU-free days were significantly lower in the massive vs minor hemorrhage group, without a difference in hospital-free days (Supplemental Table 3). Those with massive hemorrhage had a significantly higher postoperative mean pulmonary artery pressure, PVR, and total pulmonary resistance but did not have a significantly higher incidence of residual pulmonary hypertension compared with those with minor hemorrhage (Supplemental Table 4).

TABLE 4 Perioperative Findings

Findings	Control Subjects (n = 819)	Postoperative Airway Hemorrhage Subjects (n = 58)	P
Intraoperative findings			
Distal disease (University of California, San Diego level III or IV)	220 (27)	22 (38)	.09
Postoperative outcomes			
Ventilator-free days	27.0 [26.0, 27.0]	24.5 [15.8, 26.0]	<.001[a]
Intensive care unit–free days	24.0 [23.0, 26.0]	20.0 [10.0, 23.0]	<.001[a]
Hospital-free days	17.0 [13.0, 19.0]	10.5 [1.5, 14.3]	<.001[a]
Use of extracorporeal membrane oxygenation	6 (0.7)	6 (10.3)	<.001[a]
Postoperative residual pulmonary hypertension	52 (6.3)	10 (17.0)	.005[a]
Mortality	10 (1.2)	8 (13.8)	<.001[a]

[a]Statistically significant P ≤ .05. Values are n (%) or median [Q1, Q3].

When compared with control subjects, the massive hemorrhage group had a significantly higher number of female subjects and distal disease, which was not observed when comparing the minor hemorrhage group with control subjects. Preoperative hemodynamics were significantly worse in both hemorrhage groups when compared with control subjects. Postoperative hemodynamics were significantly worse when comparing the massive hemorrhage group with control subjects but did not significantly differ between the minor hemorrhage group and control subjects (Supplemental Table 5).

Mortality within the airway hemorrhage group was 13.8% (n = 8), accounting for 44.4% of all deaths among the study population. The mortality rate in the control group was significantly lower at 1.2%. Causes of death in the airway hemorrhage group included right ventricular failure from residual pulmonary hypertension (n = 3), severe reperfusion lung injury with multiorgan failure (n = 2), and other (n = 3). Among those who died, airway hemorrhage was managed with bronchial blocker and ECMO (n = 2), bronchial blocker without ECMO (n = 3), and by withholding anticoagulation alone (n = 3). The massive hemorrhage group had a higher mortality rate compared with the minor hemorrhage group (17.9% vs 10.0%, $P = .46$), and both groups had significantly higher mortality rates when individually compared with control subjects.

COMMENT

This is the first large series describing the incidence, risk factors, management, and outcomes of airway hemorrhage complicating PTE surgery. Airway hemorrhage after PTE occurred in 6.6% of our study population and was associated with a significantly elevated mortality (13.8%). Older age, female sex, history of preoperative hemoptysis, and higher preoperative PVR were all

associated with post-PTE airway hemorrhage. Moreover those with airway hemorrhage suffered from poorer postoperative outcomes, posing challenges in the perioperative management of these complex patients.

Our study identified preoperative hemoptysis as a risk factor for post-PTE airway hemorrhage, which may support the hypothesis that airway hemorrhage results from systemic-collateral vessel bleeding. It has been proposed that the proliferation and remodeling of these vessels may be due to decreased pulmonary artery pressures downstream from pulmonary artery obstruction.[7,14] The incidence of preoperative hemoptysis was similar between the minor and massive hemorrhage groups but was significantly higher when compared with control subjects. Despite these findings only a small percentage of the subjects with preoperative hemoptysis (15%) developed postoperative hemorrhage.

Preoperative hemodynamics have been identified as predictors of post-PTE complications. More severe preoperative pulmonary hypertension increases the risk of postoperative residual pulmonary hypertension, which is reported in up to one-third of patients undergoing PTE.[15-18] Residual pulmonary hypertension poses challenges in postoperative management, because it correlates with a higher risk of early all-cause mortality in the post-PTE CTEPH population.[19-21] The etiology of residual pulmonary hypertension is believed to be due to concomitant nonoperable small-vessel vasculopathy.[7] In cases where anticoagulation is withheld postoperatively, residual pulmonary hypertension may occur from recurrent thrombosis. Both severe preoperative pulmonary hypertension and a higher incidence of postoperative pulmonary hypertension were observed in our airway hemorrhage subjects.

Nonmodifiable risk factors of age and sex have been linked to poorer postsurgical outcomes in PTE patients. Although PTE surgery can be performed with an acceptable mortality in select elderly patients, older age has been associated with increased mortality and length of stay.[22,23] A case series of 8 PTE subjects with severe airway hemorrhage requiring ECMO found that those requiring ECMO were slightly older than control subjects (67 vs 60 years), and 5 of 8 patients were older than 70 years.[6] Our larger sample size supports the association between older age and increased incidence of post-PTE airway hemorrhage.

The relationship between female sex and postoperative airway hemorrhage is unclear. A comparison of sex-specific differences in the European CTEPH Registry showed that women were less likely to undergo surgery than men, primarily because of the presence of microvascular disease.[24] D'Armini and associates[25] reported a female predominance in the distal disease group of a surgical series of 331 CTEPH patients. Guth and colleagues'[6] series of patients requiring ECMO found a higher percentage of women in the postoperative airway hemorrhage group compared with those without bleeding (75% vs 45.5%). It is possible that women have a higher propensity to develop postoperative airway hemorrhage, and more specifically massive hemorrhage, because of more distal disease and microvascular involvement. Aside from sex, no preoperative factors or hemodynamic parameters significantly differed between the minor and massive hemorrhage groups, suggesting that severity of CTEPH itself may not predict the severity of airway hemorrhage.

Subjects who developed airway hemorrhage, particularly those with massive hemorrhage, more frequently had distal disease compared with control subjects. The surgical complications with resection of more distal disease are hypothesized to occur from difficulty in accessing the diseased vessels intraoperatively. Both the distal anatomic location and the fragility of pathologic tissues predispose the tissue to more injury and likely subsequent intraoperative airway bleeding.[9,11]

The role of coagulopathy in airway hemorrhage is difficult to tease out in this population. Most patients receive blood products emergently when airway hemorrhage is identified without measurement of coagulation studies. However in most subjects airway hemorrhage was localized to a particular lobe(s) with an absence of bleeding from other sites, suggesting that coagulopathy is not the cause of bleeding in most patients with airway hemorrhage.

The higher incidence of airway hemorrhage (6.6%) and the lower in-group mortality (13.8%) seen in our study compared with other previously published case series is likely related to our inclusion of less-severe cases of airway hemorrhage, an increase in complexity of cases undergoing PTE at our center, and advances in supportive interventions.[13] The difference in mortality rates between the minor (10.0%) and massive (17.9%) airway hemorrhage groups was not statistically significantly, perhaps because of the small sample size

Strategies to mitigate this severe complication of PTE have not been well studied, but given our experience we rely on a treatment algorithm starting immediately after endarterectomy is completed (Figure 2). While still on circulatory arrest and before closure of the arteriotomy, a "bubble test" is performed by turning the pulmonary artery and left atrial vents off and filling up the pulmonary vasculature with saline solution. The anesthesiologist then applies a Valsalva maneuver with a peak inspiratory pressure of 30 cm H_2O. A disruption of the vascular wall with direct communication to the airways or lung parenchyma will manifest as a continuous bubble stream. Depending on the severity of the "bubbling," the surgeon decides if direct occlusion of the affected branch is the appropriate next

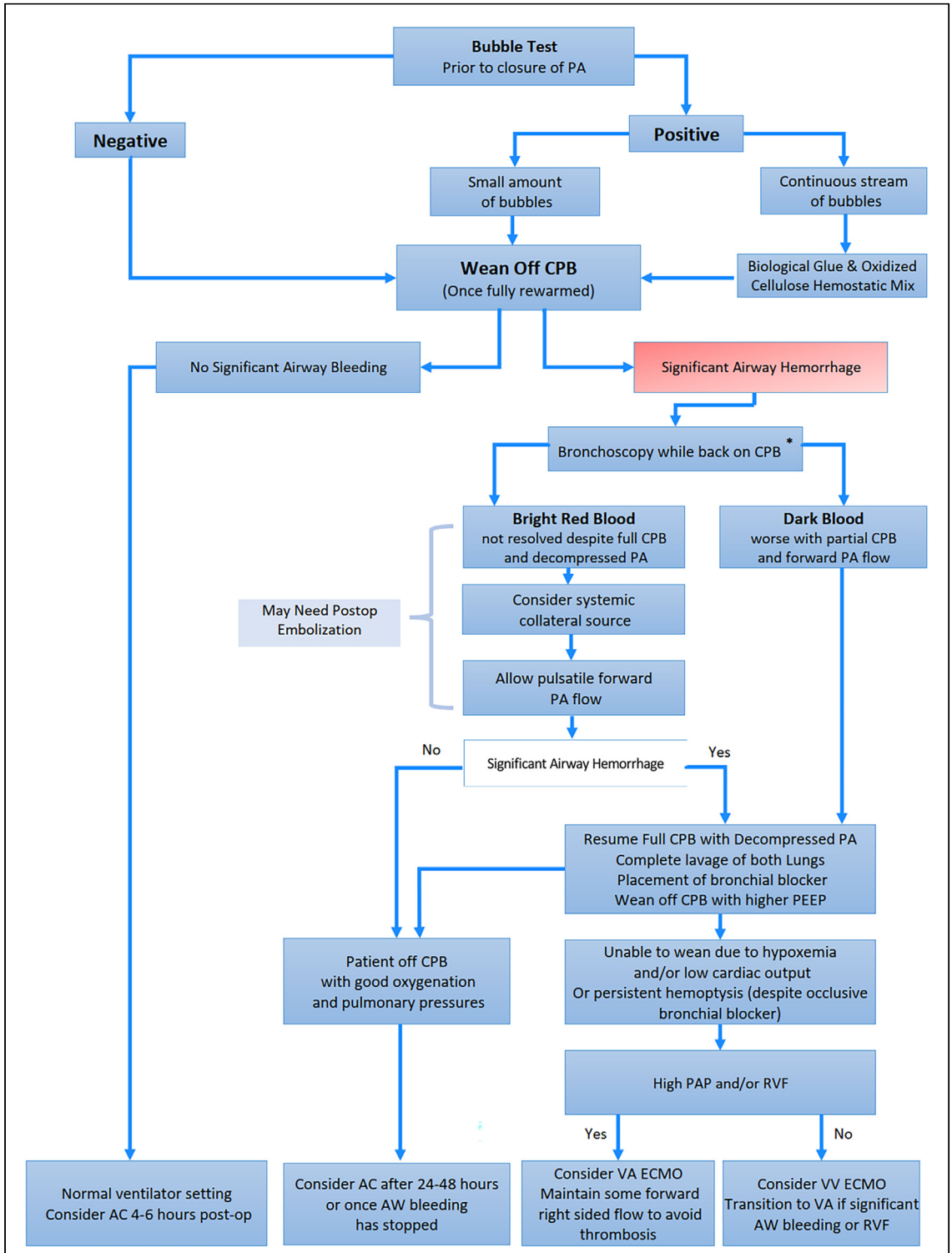

FIGURE 2 Airway hemorrhage algorithm. Flowchart showing a stepwise algorithm for diagnosis and management of intraoperative airway bleeding. *Consider changing the endotracheal tube, while on bypass, to a larger size to accommodate the bronchoscope and an endobronchial blocker if needed. (AC, anticoagulation; AW, airway; CPB, cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenator; PA, pulmonary artery; PAP, pulmonary artery pressure; PEEP, positive end-expiratory pressure; post-op, postoperatively; RVF, right ventricular failure; VA, venoarterial; VV, venoveno.)

step. In such cases we identify the affected segmental/subsegmental branch and occlude it with a mixed biologic glue and oxidized cellulose-based hemostatic agent for ease of handling and to avoid spillage of otherwise liquid glue. Care must be taken to limit the occlusive material only to the most distal segmental branch affected. This maneuver, in combination with holding anticoagulation, is effective in most patients with significant airway hemorrhage; however it does result in complete reocclusion of the affected segment(s) just opened up by endarterectomy.

If the bubble test is negative and bleeding is still encountered during rewarming and while on full cardiopulmonary bypass with no forward pulmonary flow, this may indicate a systemic-collateral communication. We have found that in these patients, the airway blood is bright red and has no relation to an empty pulmonary artery. If this is encountered, allowing forward pulsatile flow through pulmonary arteries and expedited separation from bypass, with reversal of anticoagulation, may be adequate without further mechanical intervention. When systemic arterial airway hemorrhage continues despite strategies explained below, embolization of the systemic collaterals may be required.

If airway bleeding is encountered while attempting to come off cardiopulmonary bypass, whenever forward pulmonary flow is resumed, it is best to resume full bypass and allow the anesthesiologist ample time to perform a thorough bronchoscopy, wash out any spillage in the contralateral side, and identify the location of hemorrhage. Once identified, an endoblocker can be placed (an endotracheal tube may need to be exchanged for larger size), ideally only occluding 1 lobe and allowing ventilation to the remaining lobe while bypass is weaned. However, depending on anatomy, an entire lung may have to be occluded. Separation from bypass is then attempted using higher positive end-expiratory pressure. If no further bleeding is encountered and the patient maintains adequate oxygenation and hemodynamics, heparin is reversed while an endoblocker is secured in place. The endoblocker is kept in place postoperatively, with attempts to deflate within 2 to 6 hours; if unsuccessful, deflation is attempted the following morning. Once no further hemorrhage is encountered, the balloon remains deflated and the blocker is kept in place until anticoagulation is resumed, at which point the blocker can be safely removed.

If the patient has diffuse multilobar hemorrhage or develops hypoxemia with the endoblocker, it is best to proceed with ECMO. The choice of venoveno vs venoarterial ECMO, best cannulation strategy (ie, central vs femoral), and duration of ECMO varies among patients and depends on the degree of hemorrhage and any concomitant residual pulmonary hypertension. The group in Germany has outlined an algorithm to convert all airway hemorrhage patients to ECMO using the same central cannulation sites, reversing heparin, and then allowing patients to recover while in the operating room.[6] With this strategy most patients only required 1 to 4 hours of ECMO with resolution of airway hemorrhage. Although this strategy can be quite effective, it may result in unnecessary ECMO in patients who may do well with more conservative approaches as described above.

We identify several limitations in this study. This study was done at a single CTEPH center, so the results may not be generalizable to other sites where there could be variations in surgeon experience and perioperative management. As with most retrospective analyses, there are inherent limitations such as the inability to control for confounding variables. Subjects in this study underwent PTE over a 5-year span. The preoperative, perioperative, and postoperative management of CTEPH patients undergoing PTE and the management of postoperative airway hemorrhage has changed over the years, which could not be accounted for in the analysis. In addition airway hemorrhage management was at the discretion of the clinician, so we were unable to comment on the impact of therapeutic interventions on outcomes. Finally because postdischarge hemodynamics are not routinely available to us, we arbitrarily defined residual pulmonary hypertension in this study as postoperative PVR > 400 dyn·s/cm^5 but recognize it may not adequately identify patients with residual pulmonary hypertension on longitudinal follow-up. Despite these limitations the results of this study are reflective of a large and diverse sample size and can be applicable to future practice.

In conclusion the incidence of airway hemorrhage after PTE is low but is associated with increased days of mechanical ventilation, ICU and hospital lengths of stay, incidence of residual pulmonary hypertension, and increased mortality, even in those with less-severe hemorrhage. Older age, female sex, and more severe preoperative pulmonary hypertension are all associated with an increased risk of developing postoperative airway hemorrhage. A history of preoperative hemoptysis was also identified as a predisposing factor, although only a small percentage of this cohort developed airway hemorrhage. These risk factors suggest a multifactorial cause of postoperative airway hemorrhage and may aid in identifying patients with an elevated risk of developing this perioperative complication.

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