



The Analysis Study of Risk of Bleeding in Patients Undergoing Pulmonary Procedure on Antiplatelet or Anticoagulant: A Comprehensive Systematic Review

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ABSTRACT

Background: Pulmonary procedure is considered to be a low bleeding risk procedure, platelet count and coagulation profile are usually evaluated prior to the procedure. In addition, several society guidelines recommend holding antiplatelet medications such as clopidogrel and prasugrel for 5 days prior to the procedure as well as holding one dose of unfractionated heparin prior to pulmonary procedure.

The aim: The aim of this study to show about risk of bleeding in patients undergoing pulmonary procedure on antiplatelet or anticoagulant. **Methods:** By the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. **Result:** Eight publications were found to be directly related to our ongoing systematic examination after a rigorous three-level screening approach. Subsequently, a comprehensive analysis of the complete text was conducted, and additional scrutiny was given to these articles. **Conclusion:** Pulmonary procedure on patients receiving either antiplatelet or anticoagulation therapy using the best available evidence. With this knowledge, physicians can assist patients or their substitute decision-makers in making an informed decision regarding the timing and safety of proceeding with a pulmonary procedure.

Keyword: Pulmonary procedure, antiplatelet, anticoagulant, bleeding.

INTRODUCTION

Consequent to both the increasing number of anticoagulant and antiplatelet agents and their broad range of indications, approximately 25% of patients who require a pulmonary procedure (PP) are receiving at least one antiplatelet or anticoagulant agent. For some patients, such as those taking aspirin for primary prevention of cardiovascular events or patients with a remote single episode of a venous thromboembolic event, decision-making regarding peri-procedural anticoagulation and antiplatelet management is uncomplicated. Temporary cessation of such agents is possible with minimal patient risk. For others receiving dual antiplatelet therapy (DAPT) in the setting of recent acute coronary syndrome, decision-making is more complicated since even temporary cessation of anticoagulant or antiplatelet medications may lead to catastrophic consequences. Furthermore, the urgency of PPs varies from elective to emergent. Physicians and patients

commonly make complex decisions, weighing PP urgency with the risks of temporary or no cessation of anticoagulant and antiplatelet medication.¹⁻³

The number of interventional pulmonary procedures has grown several fold over the past few years. Given the growth of these procedures and availability of newer cancer treatments, diagnostic and therapeutic applications have expanded. This growth means more procedures in medically complex patients, including those with cardiovascular diseases. Antiplatelet therapy is commonly administered for the primary and secondary prevention of cardiovascular diseases. Surprisingly, statements on interventional pulmonology from the American College of Chest Physicians and the European Respiratory Society/American Thoracic Society do not discuss the management of these medications in the peri-procedural setting. There are some guidelines on management of antithrombotic and antiplatelet agents

in patients undergoing endoscopic procedures as well as those undergoing diagnostic flexible bronchoscopy, but there are no specific guidelines to date regarding the management of antithrombotic agents in patients undergoing interventional pulmonary procedures.^{4,5}

Oral anticoagulants are used to prevent and treat thromboembolic disease in patients with mechanical cardiac valve, atrial fibrillation (AF), stroke, deep venous thrombosis, and pulmonary emboli. For years, vitamin K antagonists (VKA) have been the main antithrombotic agents. Newer oral anticoagulation agents (NOAC) such as dabigatran, rivaroxaban, apixaban and edoxaban have been introduced into clinical practice starting in 2010 and have been adopted rapidly by the physicians. For AF the use of the NOAC has matched the use of warfarin in 2014. Oral antiplatelet therapy such as aspirin and clopidogrel is widely used to prevent arterial thrombosis such as heart attacks, strokes and in-stent thrombosis. It is estimated that over 30% of the adult population uses

aspirin for primary or secondary prevention of cardiovascular disease. Thus, the practicing pulmonologist is likely to encounter a patient using at least one of these agents and requiring a bronchoscopy. Balancing the risk of bleeding during bronchoscopy to the risk of thrombosis while withholding these agents is the corner stone of the peri-procedural management of anticoagulation therapy.⁶⁻⁹

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we compare and contrast risk of bleeding in patients undergoing pulmonary procedure on antiplatelet or anticoagulant. It is possible to accomplish this by researching of the risk of bleeding in patients

undergoing pulmonary procedure on antiplatelet or anticoagulant. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine about the risk of bleeding in patients undergoing pulmonary procedure on antiplatelet or anticoagulant. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2014, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "risk of bleeding in patients undergoing pulmonary procedure on antiplatelet or anticoagulant." as keywords. The search for studies to be included in the systematic review was carried out using the PubMed, SagePub, and Sciencedirect databases.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and cannot have been seen anywhere else.

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search.

We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations

were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

Table 1. Search Strategy

<i>Database</i>	<i>Search Strategy</i>	<i>Hits</i>
Pubmed	((("Pulmonary procedure"[MeSH Subheading] OR "Antiplatelet"[All Fields] OR "Anticoagulant" [All Fields]) AND ("Management"[All Fields] OR "Therapy"[All Fields]) AND ("Outcome"[All Fields]) OR ("Bleeding" [All Fields]))	2019
Science Direct	((("Pulmonary procedure"[MeSH Subheading] OR "Antiplatelet"[All Fields] OR "Anticoagulant" [All Fields]) AND ("Management"[All Fields] OR "Therapy"[All Fields]) AND ("Outcome"[All Fields]) OR ("Bleeding" [All Fields]))	89
Sagepub	((("Pulmonary procedure"[MeSH Subheading] OR "Antiplatelet"[All Fields] OR "Anticoagulant" [All Fields]) AND ("Management"[All Fields] OR "Therapy"[All Fields]) AND ("Outcome"[All Fields]) OR ("Bleeding" [All Fields]))	347

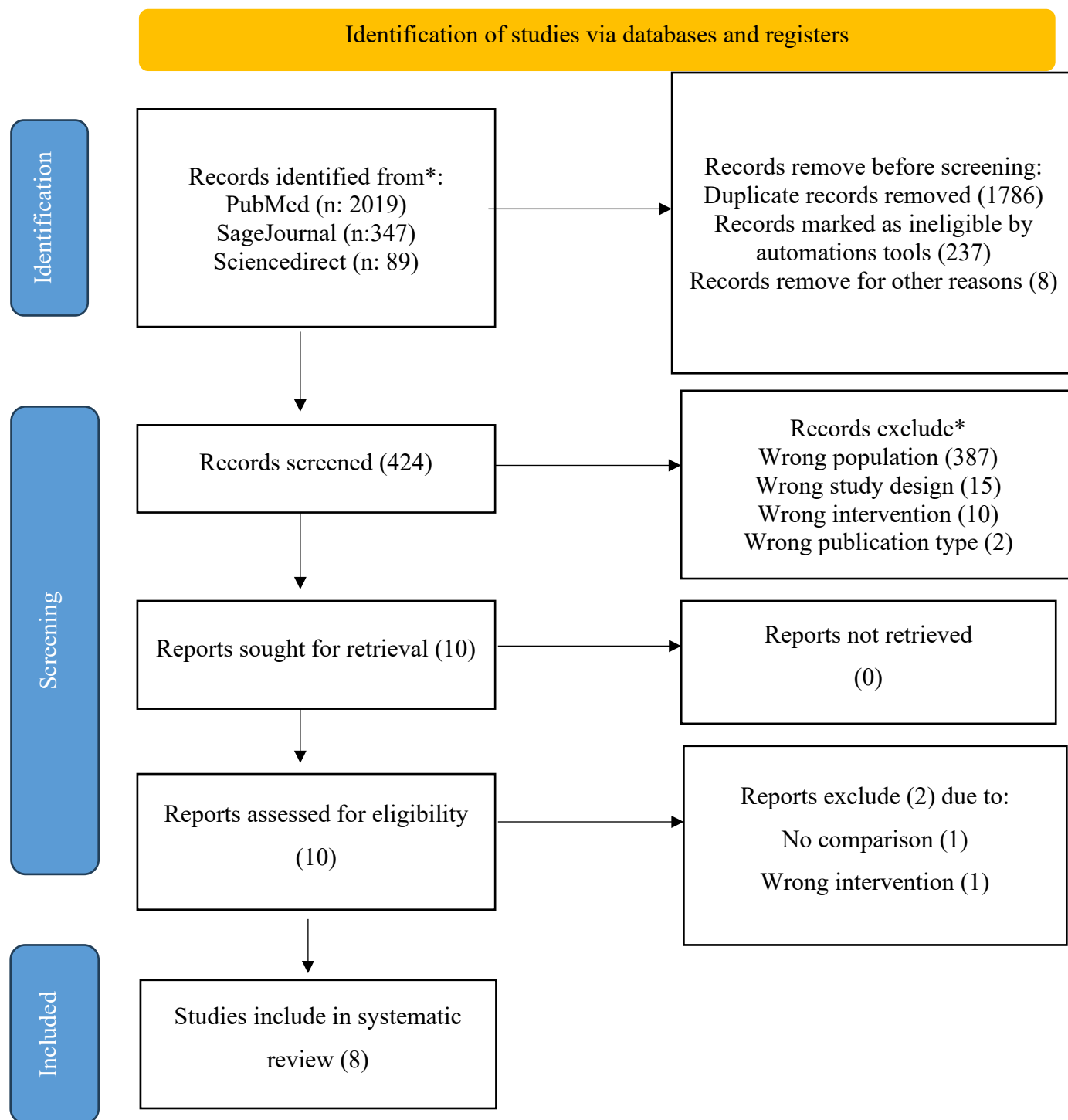


Figure 1. Article search flowchart

Table 2. Critical appraisal of Study

Parameters	(Aljundi, L et al., 2021)	(Dang ers, L et al., 2021)	(Perl, S et al., 2020)	(Patel, pp et al., 2019)	(Harri s,K et al., 2016)	(Meena , N et al., 2016)	(Mah mood , K et al., 2014)	(Hong, HJ et al., 2024)
1. Bias related to temporal precedence								
Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation								
Was there a control group?	No	No	Yes	No	Yes	No	Yes	Yes
3. Bias related to confounding factors								
Were participants included in any comparisons similar?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Bias related to administration of intervention/exposure								
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	No	No	No	No	No	No	No	No
5. Bias related to assessment, detection, and measurement of the outcome								
Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	No	No	No	No	No	No	No	No
Were the outcomes of participants included in any comparisons measured in the same way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Bias related to participant retention								
Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Statistical conclusion validity								
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

RESULT

Using reputable resources like Science Direct, PubMed, and SagePub, our research team first gathered 2455 publications. A thorough three-level screening strategy was used to identify only eight papers as directly relevant to our ongoing systematic evaluation. Next, a thorough study of the entire text and further examination of these articles were selected. Table 3 compiles the literature that was analyzed for this analysis in order to make it easier to view.

Table 3. The literature include in this study

Author	Origin	Method	Sample	Result
Aljundi, L et al., 2021 ¹⁰	USA	This is a retrospective descriptive study that included 292 patients who underwent thoracentesis in the inpatient setting at Ascension St John Hospital in Detroit, Michigan, USA from 2016 to 2018.	292	Two hundred and ninety-two thoracenteses were performed, 95.5% (n=279) were performed by interventional radiology. Majority of patients were at risk of bleeding 83% (n=242). No bleeding events occurred. Medications that were not held prior to thoracentesis included: clopidogrel 11% (n=32), novel anticoagulants 8.2% (n=24) and unfractionated heparin 50% (n=146). Use of ultrasound guidance decreased the amount of haemoglobin decline from 1 to 2 g/L (p=0.029). Seventeen patients suffered pneumothorax, eight of which required intervention.
Dangers, L et al., 2021 ¹¹	France	We conducted a French multicenter cohort study in 19 centers. The main outcome was the occurrence of bleeding, defined as hematoma, hemoptysis or hemothorax, during the 24 hours following the pleural procedure.	1124	A total of 1124 patients was included (66% of men, median age of 62.6 ± 27.7 years), of whom 182 were on antiplatelet therapy and 942 were not. Fifteen patients experienced a bleeding event including eight serious bleedings. The 24-hour incidence of bleeding was 3.23% (95% CI, 1.08 to 5.91) in the antiplatelet group and 0.96% (95% CI, 0.43 to 1.60) in the control group. The occurrence of bleeding events was significantly associated with antiplatelet therapy in univariate (OR, 3.44; 95% CI, 1.14 to 9.66; p=0.021) and multivariate analysis (OR, 4.13; 95% CI, 1.01 to 17.03; p=0.044) after adjusting for demographic data and the

				main risks factors for bleeding. Likewise, antiplatelet therapy was significantly associated with 19 serious bleeding in univariate (OR, 8.61; 95% CI, 2.09 to 42.3; $p=0.003$) and multivariate analysis (OR, 7.27; 20 95% CI, 1.18 to 56.1; $p=0.032$) after adjusting for the number of risk factors for bleeding.
Perl, S et al., 2020¹²	Israel	Retrospective chart review of hospitalized patients undergoing thoracentesis with or without clopidogrel treatment.	257	The study group comprised of 88 cases and 169 controls. Four bleeding complications were noted in the cases group, versus 5 in the control group (RR 1.53, 95% CI 0.4–5.5).
Patel, pp et al., 2019¹³	USA	A retrospective analysis was performed of ultrasound-guided thoracenteses completed at an academic institution between January 1, 2016, and November 14, 2017.	115	A total of 115 thoracenteses were performed in 103 patients actively taking an NOAC (n¼43) and/or clopidogrel (n¼69). All patients used either the NOAC or clopidogrel within 24 hours before the procedure and continued using it daily thereafter. There were no bleeding complications.
Harris,K et al., 2016¹⁴	USA	This was a retrospective study to determine if there was a higher risk of bleeding in patients on aspirin undergoing therapeutic bronchoscopy compared with those not on aspirin.	108	Of the 108 patients who had multimodality therapeutic bronchoscopy, 17 (15.7%) were taking aspirin and 91 (84.3%) were not on aspirin. Patients in the aspirin group were older than those in the no aspirin group (median age: 66 <i>versus</i> 60 years, $p = 0.007$). The treatment modalities were similar in both groups except that more patients in the no aspirin group were treated with argon plasma coagulation (APC) compared to the aspirin group (60.4% <i>versus</i> 29.4%, $p = 0.031$). The estimated blood loss (EBL) between

				the aspirin and no aspirin groups was not significantly different (mean: 6.0 <i>versus</i> 6.7 ml; median: 5.0 <i>versus</i> 5.0, $p = 0.36$). Overall, there was no difference in complications between both groups.
Meena, N et al., 2016 ¹⁵	USA	Retrospective review of sequential cases of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and esophageal ultrasound fine needle aspiration (EUS-FNA).	395	Three hundred ninety-five consecutive procedures were reviewed. Thirty-seven patients were taking clopidogrel at time of biopsy. The patients taking clopidogrel were significantly older than those in the control group. Two patients (1%) in the control group were admitted for observation, but neither was found to have a significant bleed. There were no clinically significant bleeding complications in either of the study groups. Conclusions:
Mahmood, K et al., 2014 ¹⁶	UK	Twenty-five consecutive adult patients who were taking clopidogrel at the time they were offered thoracentesis or small-bore (14 Fr) chest tube placement consented to continue taking the drug through their procedure. A control group consisted of 50 patients undergoing these pleural procedures who were not taking clopidogrel at the time they consented to undergo either procedure.	75	There was one case of hemothorax after thoracentesis in the clopidogrel group versus none in the control group. The one patient with hemothorax required transfusion with 2 units of packed red blood cells and small-bore chest tube placement, and clopidogrel was withheld. There were no other clinically apparent complications of either procedure.

Hong, HJ et al., 2024 ¹⁷	Korea	We retrospectively reviewed a cohort of 498 elderly patients who underwent surgery for lung cancer. These patients were categorized into 2 groups group N, which did not receive antiplatelet therapy, and group A, which did.	488	There were 387 patients in group N and 101 patients in group A (Ai 70, Am 31). No significant differences were found in intraoperative blood loss, thoracotomy conversion rates, transfusion requirements, volume of chest tube drainage, or reoperation rates for bleeding control between groups N and A or between groups Am and Ai. The duration of hospital stay was longer for group A compared to group N (7 days vs. 6 days, $p=0.005$), but there was no significant difference between groups Ai and Am. The incidence of cardiovascular or cerebrovascular complications did not differ significantly between groups Ai and Am. However, group Ai included a severe case of in-hospital ST-elevation myocardial infarction.
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DISCUSSION

Antiplatelet therapy with aspirin and clopidogrel or clopidogrel alone has been shown to increase the risk of bleeding after transbronchial biopsies. In a small retrospective case series, dual antiplatelet therapy was safely continued in patients undergoing endobronchial ultrasound guided transbronchial aspiration. Most diagnostic and therapeutic bronchoscopies are performed while patients are receiving aspirin with no increased risk of bleeding. There is no data however on performing endobronchial biopsies in patients on dual antiplatelet therapy.^{18,19}

Thoracentesis, pleural biopsy, catheter or chest tube drainage, and thoracoscopy are the main pleural procedures in the area of pleural diseases. Considering the bleeding risk associated with specific pleural procedures, the risk is low for thoracentesis, moderate for insertion or removal of chest tube or tunneled catheter, and moderate-high for pleural biopsies and thoracoscopy. We make certain recommendations to reduce the risk of bleeding

complication. These include the use of a patient checklist before pleural procedures, cognizance related to pharmacokinetics of antithrombotic and antiplatelet agents, image-guidance, and experience.^{20,21}

Diagnostic and therapeutic bronchoscopies have long been performed on aspirin with no reported increased risk of bleeding complications. A recent retrospective review of 12 patients showed that endobronchial ultrasound guided transbronchial aspiration was safely performed on dual antiplatelet therapy with aspirin and clopidogrel. In a prospective study of transbronchial biopsies performed on aspirin and clopidogrel versus clopidogrel alone, the risk of significant bleeding was very high at 100% and 89% respectively. All patients in the aspirin and clopidogrel group developed moderate to severe bleeding but no fatalities or surgical interventions were reported. However, endobronchial biopsy in patients receiving dual antiplatelet therapy is not well described in the literature. In many patients with recent coronary artery stenting, early

discontinuation of dual antiplatelet therapy prior to an elective invasive procedure exhibits a high risk of life-threatening stent thrombosis.^{18,22}

Stamenovic *et al.* evaluated the perioperative use of aspirin in patients undergoing major lung resections. Before this study, there had been only a few retrospective studies with relatively small numbers of patients in the field of thoracic surgery. Among a total of 486 patients, 329 did not use aspirin (group ASA-0), while 157 did (group ASA-1), in the perioperative period. Two hundred and seventy-three patients (56.2%) underwent video assisted thoracoscopic surgery (VATS) and 213 (43.8%) underwent thoracotomies. There was no difference in the surgical approach (VATS vs. thoracotomy) and type of surgical resection between the groups. In terms of postoperative outcomes, there was no difference in intraoperative bleeding, blood loss, blood transfusion, thoracotomy conversion from VATS, cardiovascular complications, and death between the groups.^{23–25}

CONCLUSION

In conclusion, pulmonary procedure on patients receiving either antiplatelet or anticoagulation therapy using the best available evidence. With this knowledge, physicians can assist patients or their substitute decision-makers in making an informed decision regarding the timing and safety of proceeding with a pulmonary procedure.

DISCLOSURE STATEMENT

Disclosure Statement : The authors have no conflicts of Interest to declare.

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