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Absorbable Powder Haemostat Use in Minimally Invasive Thoracic Surgery

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Absorbable Powder Haemostat Use in Minimally Invasive Thoracic Surgery

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Abstract: Background: Significant intraoperative and postoperative blood loss are rare but possibly life-threatening complications after lung resection surgery either during open or minimally invasive procedure. Microporous Polysaccharide Hemospheres (ARISTA™AH) have demonstrated time-efficient haemostasis, lower post-operative blood volumes and a lower blood transfusion requirement, without any identified adverse events across other specialities.The primary aim of our study was to evaluate the impact of haemostatic agents on short-term postoperative outcomes in thoracic surgery. Methods: We retrospectively reviewed a prospectively collected database of consecutive early-stage lung cancer patients surgically treated in two European centres(October 2020-December 2022).Exclusion criteria:open surgery,patients with coagulopathy/anticoagulant medication,major intraoperative bleeding,non-anatomical lung resection and age <18 years.The cohort was divided into 5 groups according to the haemostatic agent used.Propensity score matching was used to estimate the effect of ARISTA™AH on various intra- and post-operative parameters(continuous and binary outcome modelling). Results:482 patients(M/F:223/259; VATS 97/RATS 385)with a mean age of 68.9(±10.6)years were analysed.In 253 cases ARISTA™AH was intraoperatively used to control bleeding.This cohort of patients had a significant reduction in total drain volume by 135 mls(standard error 53.9; p=0.012).The use of ARISTA™AH did reduce the average length of hospital stay(-1.47 days)and duration of chest drainage(-0.596 days)albeit not significant.In the ARISTA™AH group,we observed no postoperative bleeding,no blood transfusion required,no 30-day mortality and no requirement for redo-surgery.The use of ARISTA™AH significantly reduced the odds of post-operative complications,need for transfusion and redo surgery. Conclusion: Our data showed that Microporous Polysaccharide Hemospheres are a safe and effective haemostatic device.Its use has a positive effect in short term postoperative outcomes of patients surgically treated for early-stage lung cancer.

Keywords: haemostatic agent; haemostatic powder; minimally invasive surgery; lung cancer; short term outcomes

1. Introduction

Minimally invasive surgical (MIS) approaches have significantly improved thoracic surgical practice, backed by randomised evidence, they now represent the gold standard surgical approach in early-stage lung cancer treatment [1,2]. Notwithstanding the important advantages conferred by MIS and the technical and technological improvements, the incidence of complications is still high (24–41%), with a major complication rate of 1.5% [3].

Among complications, increased haemorrhagic output or postoperative bleeding may increase the risk of re-operation, retained effusion which also affect length of chest drain and length of stay.[4]

Effective intraoperative haemostasis can help to reduce the risks of serious complications, to prevent infections and to reduce the hospitalization. For those reasons, blood loss management is an important task and several haemostats have been developed to help surgeons to minimise the blood loss and the risk of bleeding. [5,6]

Topical haemostatic agents are applied for bleeding control during surgery when conventional methods (e.g. compression, ligation, clipping and electrocautery) are impractical or insufficient. Several haemostats, such as synthetic glues, liquid fibrin sealants, powder, oxidised cellulose fleece and cotton gauze are commonly used to help achieving haemostasis [7–9].

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In 2021 a position paper was published on the use of haemostatic powder in several specialties: general surgery, gynaecology, urology, breast and thoracic surgery. [10]

According to the available literature, there have been very few controlled clinical studies or large retrospective cohort analyses to assess the efficacy and safety of topical haemostatic agents in thoracic surgery.

Referring to thoracic surgery, applications during lymphadenectomy, decortication of the pleura and lung transplantation in patients on extracorporeal membrane oxygenation (ECMO) have been considered. A steering group of multidisciplinary European surgeons formulated twelve recommendations on the use of haemostatic powder, showing its safety and efficacy [10].

Moreover, the Italian society of thoracic surgeons (SICT) drew up a Delphi consensus on air leak and intraoperative bleeding. Concerning the haemostats, the panel of experts reported that the routine intraoperative use of topical haemostats are indicated for: modest bleeding/hematoma of the pulmonary artery and slow ooze; haemostasis of vascular sutures; haemostasis of particularly "sensitive" areas (e.g., close to the oesophagus/phrenic/recurrent nerves); parenchymal losses and bleeding from the parenchymal suture line; area of mediastinal lymphadenectomy, small bleeding during lymphadenectomy; after parietal pleurectomy or decortication[11].

Since there are many different operations and haemostats available, it is mandatory that the surgeons know each product in order to identify the optimal haemostatic agent for each procedure (Table 1).

Table 1. Summary of Haemostatic products.

Group	Category	Active principle	Example
ACTIVE	Thrombin	Bovine derived thrombin Human plasma derived thrombin with porcine gelatine sponge Recombinant thrombin	Thrombin-IMI® Evithrom® Recothrom®
	Collagen	Collagen	Avitene™ MCH Helistat® Helitene®
COMBINED	Thrombin + Mechanical agent	Gelatine plus thrombin	Floseal® Gelfoam® Vitagel®
	Fibrin sealant	Human Plasma derived Human pooled plasma and equine collagen	Tisseel® Vistaseal®
NON-ACTIVE	Mechanical Haemostatic Agents	Porcine gelatine Oxidized cellulose Polysaccharide spheres	Surgiflo® Surgifoam® Surgicel® (Tabotamp) ARISTA™ AH

The aim of the present study is to evaluate the safety and efficacy of ARISTA™ haemostatic polysaccharide hemosphere and to compare this specific product with others haemostatic agents currently used in thoracic surgery.

2. Materials and Methods

All consecutive patients who received elective minimally invasive surgery for early-stage non-small cell lung cancer (NSCLC) in two European centres (S. Camillo Forlanini Hospital (Rome, Italy) and Guys Hospital (London, UK) from October 2020 to December 2022 were included in the study.

Indications, preoperative examinations and criteria for performing minimally invasive surgery were in the line with the standard set out by the NCCN guidelines.

The type of surgical approach (VATS or RATS) was chosen according to surgeons' preference. All robotic lobectomies were performed with Da Vinci Xi platform, with a standard totally endoscopic technique, through four intercostal incisions, under CO2 insufflation (5–8 mmHg), without utility incision. In 169 cases an extra utility port (15 mm trocar) was used. The VATS lobectomies were performed with bi-portal or tri-portal approach as the standard D'Amico or Copenhagen approaches [12,13].

Data Collection

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Data on patients intraoperatively treated with haemostats were prospectively recorded. Demographic, clinical, surgical, and pathological data were then retrospectively analysed from the surgical registry. All patients were stratified according to the haemostatic agent used during surgery.

We excluded patients who underwent open surgery or who underwent wedge resection; patients with coagulopathy or anticoagulant medication; patients <18 years. Additional exclusion criteria comprised history of allergic reactions after application of human fibrinogen, human thrombin or collagen of any origin. Patients who experienced major intraoperative bleeding due to vascular injury were also excluded.

The haemostatic agents used during surgery were:

- ARISTA™ AH (BD, New Jersey, USA) is a surgical haemostatic powder derived from purified plant starch. Its Microporous Polysaccharide Hemospheres are typically absorbed in 24-48 hours. It's thrombin free, biocompatible and non-pyrogenic agent.
- Surgicel® (Ethicon, New Jersey, USA) is a resorbable, sterile haemostatic agent in oxidized and regenerated cellulose (Rayon). Complete absorption in 1/2 weeks.
- TachoSil® (Corza Medicsl, US) is a sterile patch, ready-to-use haemostatic agent. It consists of an equine collagen patch coated with human fibrinogen and human thrombin. Complete absorption in 3/4 weeks.
- Hemopatch® (Baxter, Illinois, USA) is an absorbable collagen pad intended for sealing and hemostasis. Complete absorption in 6/8 weeks.

According to the intraoperatively used haemostats, the whole cohort was divided into 5 groups (Table 2). The number of haemostats application was dependent upon bleeding and at the discretion of the surgeon. Endpoints evaluated included: surgical time and haemostatic time, intraoperative blood loss, chest tube output at 24 hours postoperatively and the total chest tube output, intra or postoperatively blood products required, length of stay, 30-day morbidity and 30-day mortality. Morbidity analysed included blood transfusion, cardiovascular shock and ICU stay>24 hours (with hypotension), renal failure (new onset requiring dialysis), sepsis (positive blood cultures and hypotension), any other postoperative complications.

According to a shared protocol, chest tube was removed as soon as no "air leak" was reported and when the fluid output was lower than 250 ml/day. The patient was usually discharged the day after the chest tube removal. Prolonged "air leak" was considered >5 days.

Statistical Analysis

Data were retrospectively collected in a computerized database and analysed with SPSS software version 11.0.1 for Windows (SPSS Inc, Chicago, IL) under the guidance of a departmental statistician. Continuous data is presented as the mean ± standard deviation or with median and interquartile range (IQR) depending on the distribution of the data, and compared through the student t test assuming unequal variances.

Propensity score matching was used to estimate the effect of ARISTA™ AH on various intra- and post-operative parameters (continuous and binary outcome modelling). The propensity scores were estimated using logistic regression based on Age, Sex, Comorbidities, Previous Cancer, Previous Lung Cancer, Tumour location, Surgeon expertise, Approach, Extent of Resection, Energy usage and Application site. One-to-one nearest neighbour matching was used. 450 patients from the original 482 patient cohort were matched according to ARISTA™ AH use (yes/no). Good balance was achieved between the ARISTA™ AH and non- ARISTA™ AH group, with all standardized mean differences below 0.2 after matching, all standardized mean differences for squares and two-way interactions between covariates were below .15, indicating adequate balance.

To estimate the effect of ARISTA™ AH on outcomes, logistic and linear regression modelling were employed according to data distribution of the outcome variable with ARISTA™ AH use as the exposure, along with covariates and their interaction as predictors. We included full matching weights in the estimation. The comparisons () function in the marginal effects package was used to perform g-computation in the matched sample to estimate the average treatment effect of the treated population (ATT). A cluster-robust variance was used to estimate its standard error with matching stratum membership as the clustering variable.

All analyses were conducted using R 4.2.3 and the MatchIt, cobalt, sandwich, lmtest and marginal effects packages [14–18].

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Ethical Statement

This study is a retrospective analysis of standard surgical procedures, was conducted in accordance with the Declaration of Helsinki and approved by our internal institutional review board (IRB).

3. Results

We included 482 patients without significant difference in preoperative characteristics (age, sex, comorbidities, procedure type) between the groups. All patients' characteristics are summarized in Table 2.

Table 2. Patients characteristics.

	All		ARISTA	SURGICEL	ARISTA+SURGICEL	ARISTA+PATCH	SURGICEL+PATCH	p-value
N		482	226	121	23	4	105	
Sex(male)	223	223 (46.3)	113 (50)	42 (34.7)	14 (60.9)	2 (50)	51 (48.6)	0.041
Age Mean(SD) Median(IQR)		68.9 (10.6) 70 (63-76)	67.1 (10.8) 69 (61-75)	69.9 (9.1) 71 (65-76)	72.7 (7) 73 (67-78)	75.8 (8.4) 76 (69-83)	71 (11.2) 72 (67-79)	0.002
Patients with comorbidity(%)		320 (70.0)	144 (68.6)	115 (95)	15 (65.2)	4 (100.0)	70 (72.2)	ns
Pulmonary(COPD, IPF)		309 (66.9)	70 (33.8)	110 (90.9)	9 (39.1)	2 (50.0)	95 (90.4)	<0.001
Hypertension		350 (76.3)	105 (51.5)	100 (82.6)	14 (60.9)	3 (75)	60 (57.1)	<0.001
Renal(CKD)		245 (53.0)	11 (5.3)	12 (9.9)	6 (26.1)	0 (0)	15 (14.3)	<0.001
Diabetes		262 (57.2	30 (14.5	18 (14.8)	7 (31.8)	0 (0)	10 (9.5)	<0.001
Other		283 (61.3)	50 (24.2)	12 (9.9)	5 (21.7)	0 (0)	9 (8.5)	<0.001
Previous cancer		148 (31.9)	71 (34.0)	38 (31.4)	6 (26.1)	1 (25)	31 (29.8)	ns
Postoperative complications(%)		153 (31.7)	51 (22.6)	44 (36.4)	7 (30.4)	0 (0)	51 (48.6)	<0.001
Prolonged Air leak		45 (9.3)	14 (6.1)	9 (7.4)	4 (17.0)	0 (0)	18 (17.1)	<0.001
Infection/Chylothorax		23 (4.7)	6 (2.6)	8 (6.6)	1 (4.3)	0 (0)	8 (7.6)	ns
Atrial fibrillation		28 (5.8)	9 (4)	7 (5.8)	1 (4.3)	0 (0)	11 (10.5)	ns
Lung atelectasis/ respiratory failure		27 (5.6)	8 (3.5)	9 (7.4)	1 (4.3)	0 (0)	9 (8.5)	ns
Ileus		22 (4.6)	11 (4.8)	7 (5.8)	0 (0)	0 (0)	4 (3.8)	ns
Unexpected ICU readmission(%)		8 (1.6)	3 (1.3)	4 (3.3)	0 (0)	0 (0)	1 (0.9)	ns
Stroke		2 (0.4)	1 (0.4)	1 (0.8)	0 (0)	0 (0)	0 (0)	ns
Acute renal injury		2 (0.4)	1 (0.4)	1 (0.8)	0 (0)	0 (0)	0 (0)	ns
Pneumonia and respiratory failure		4 (0.8)	1 (0.4)	2 (1.6)	0 (0)	0 (0)	1 (0.9)	ns

The great majority of procedures were lobectomy (328, 68%) and a robotic assisted procedure was used in 385 patients (80%).

In all 482 patients, haemostasis was reached using a haemostatic agent: ARISTA™ AH alone was used in 226 cases, SURGICEL in 121, a combination of ARISTA and SURGICEL in 23, a combination of ARISTA and patch in 4, a combination of SURGICEL and patch in 105.

All the haemostatic agents are ready to use, so there was no time needed to prepare the haemostats. The application of both patches (Tachosil and Haemopatch) lasted 2-3 minutes, while ARISTA and SURGICEL were applied and left in the blood loss site.

The median surgical time was 100 minutes (IQR 80-120) with a median haemostatic time of 3 minutes (IQR 2-8).

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The patches (Tachosil and Haemopatch) were applied in 109 cases, when a lung injury occurred causing air leak. The haemostatic agents were generally applied to control the bleeding in the lymphadenectomy sites (367 patients; 76%). In 115 patients (24%) the haemostats were used in different sites (e.g. minor bleeding on hilar vessels, oozing from parenchymal stapler line, oozing from pleural adherences).

The great majority of patients (467; 87%) had only one chest drain (24 or 28 Ch), while 15 (3%) had two drainages (28 Ch). The median chest tube duration was 3 days (IQR 1-4) and the median hospital stay was 5 days (IQR 4-7).

Postoperative complications were reported in 153 patients (31.7%). No 30- and 90-day mortality occurred, no allergic reactions to the haemostatic agents were reported.

On post-operative day one (POD#1) the fluid was haemoserous in 98%, in 7 cases sanguineous and in 2 cases chyle was noticed.

The median quantity of fluid at first day was 150 ml (IQR 93-271) and the median total amount of drain was 340 ml (IQR 200-600) (Table 3)

Table 3. Intra and postoperative variables.

	All	ARISTA	SURGICEL	ARISTA+SURGICEL	ARISTA+PATCH	SURGICEL+PATCH
N	482	226	121	23	4	105
Duration of surgical procedure, min Mean (SD) Median (IQR)	105.8 (36.0) 100 (80 ; 120)	103.0 (40.8) 90 (70 ; 120)	102.2 (25.9) 100 (90 ; 120)	132.2 (53.7) 120 (80 ; 175)	96.2 (21.7) 102 (91 ; 107)	109.9 (28.0) 110 (90 ; 120)
Intraoperative blood loss Mean (SD) Median (IQR)	44.9 (62.9) 20 (10 ; 50)	43.3 (61.8) 20 (10 ; 50)	41.0 (65.0) 20 (10 ; 50)	101.3 (94.2) 80 (50 ; 100)	33.8 (31.5) 22 (17 ; 39)	41.9 (50.1) 20 (10 ; 50)
Hospitalization, Day Mean (SD) Median (IQR)	6.6 (6.6) 5 (4 ; 7)	5.4 (3.3) 5 (3 ; 6)	7.2 (7.1) 5 (4 ; 8)	6.2 (1.8) 6 (5 ; 6)	5.2 (2.1) 5 (4 ; 6)	8.6 (10.2) 7 (4 ; 10)
Chest tube duration, Day Mean (SD) Median (IQR)	4 (4.7) 3 (1;4)	3.6 (3.5) 3 (1; 4)	3.9 (4.6) 3 (1;4)	5 (1.7) 5 (4;5)	1.5 (1.0) 1 (1;1)	4.7 (6.9) 2 (1;4)
Total amount of drain, ml Mean (SD) Median (IQR)	464.3 (439.6) 340 (200 ; 600)	355.2 (328.4) 250 (160 ; 400)	544.9 (604.5) 425 (260 ; 600)	848.0 (369.4) 800 (675 ; 1000)	183.8 (214.4) 82 (72 ; 194)	521 (390.4) 445 (232 ; 702)
Quantity of fluid at first day, ml Mean (SD) Median (IQR)	200.9 (171.9) 150 (93 ; 271)	139.8 (140.3) 100 (50 ; 150)	269.9 (204.3) 200 (150 ; 345)	321.7 (136.4) 300 (250 ; 400)	132.5 (112.1) 82 (72 ; 142)	226.0 (153.4) 200 (110 ; 300)
Patients with comorbidity (%)	320 (70.0)	144 (68.6)	87 (72.5)	15 (65.2)	4 (100.0)	70 (72.2)

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Surgeon, Fellow (%)	52 (10.8)	33 (14.6)	10 (8.3)	4 (17.4)	0 (0.0)	5 (4.8)
Prolonged Air leak, (%)	7 (2.2)	3 (4.8)	0 (0.0)	3 (13.0)	- (-)	1 (1.0)
Surgical Procedure - Lobectomy (%) - Segmentectomy (%)	328 (68.0) 154 (32.0)	152 (67.3) 74 (32.7)	83 (68.6) 38 (31.4)	18 (78.3) 5 (21.7)	2 (50.0) 2 (50.0)	73 (69.5) 32 (30.5)
Energy device						
- no	385 (80.7)	168 (74.3)	101 (87.1)	5 (21.7)	4 (100.0)	104 (99)
- ligasure	66 (13.8)	40 (17.7)	13 (11.2)	12 (52.2)	0 (0.0)	1 (1.0)
- harmonic	26 (5.5)	18 (8.0)	2 (1.7)	6 (26.1)	0 (0.0)	0 (0.0)
Quality first day						
- serum-hematic (%)	414 (97.9)	166 (99.4)	117 (96.7)	19 (82.6)	4 (100.0)	105 (100.0)
- hematic (%)	7 (1.7)	1 (0.6)	2 (1.7)	4 (17.4)	0 (0.0)	0 (0.0)
- chylus (%)	2 (0.5)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)

Six patients underwent redo surgery (2 for bleeding, 1 for oncological reasons and 3 for air leaking). No bleeding, blood transfusion or redo-surgery had been observed in ARISTA™ AH group.

Eleven covariates were employed for matching as detailed in the methodology. Distribution of propensity scores and covariate balancing are displayed in supplementary figures1 and 2.

Univariate Linear Regression Modelling

We explored the effect of ARISTA™ AH application on length of stay(days), intra-operative blood loss(mls), duration of surgery(mls), chest drain duration(days) and total drain volume loss(mls) using a linear regression model in a univariate manner. The use of ARISTA™ AH application resulted in a significant reduction in total drain volume by 135 mls (standard error 53.9; p=0.012). The use of ARISTA™ AH did reduce the average length of hospital stay (-1.47 days) and duration of chest drainage (-0.596 days) albeit not significant (Table 4).

Table 4. Univariate and multivariate Linear Regression modelling.

Variable	Estimate	SE	95% CI	p-value
UNIVARIATE				
Length of stay (days)	-1,47	0.806	-3,05-0,108	0,068
Intraoperative blood loss (mls)	9,42	5,99	-2,31-21,2	0,115
Duration of surgery (mins)	1,01	3,44	-5,73-7,76	0,769
Chest drain durations (days)	-0,596	0,462	-1,5-0,31	0,198

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Total drain volume (mls)	-135	53,9	-241-29,5	0,012
MULTIVARIATE				
Length of stay (days)	-0,792	0.85	-2,46-0,873	0,351
Intraoperative blood loss (mls)	0,533	9,13	-17,4-18,4	0,953
Duration of surgery (mins)	-0,981	3,52	-7,87-5,91	0,351
Chest drain durations (days)	-0,572	0,24	-1,6-0,455	0,275
Total drain volume (mls)	-126	79,4	-282-29	0,111

Multivariate Regression Modelling with Covariate Interaction

Length of stay, intra-operative blood loss, duration of surgery, chest drain duration and total drain volume loss using a linear regression model in a multivariate manner were not significantly impacted by Arista application (Table 4).

We explored the impact of Arista use on intra-operative complications, post-operative complications, Haemoglobin loss or need for transfusion and need for redo-operation (Table 5). Use of Arista significantly reduced the odds of post-operative complications, need for transfusion and redo-surgery.

Table 5. Multivariate Logistic Regression modelling with Covariate Interaction.

Variable	Estimate (Odds Ratio)	95% CI	p-value
Intraoperative compliactions	1	1-1	NS
Postoperative complications	0,383	0,248-0,591	<0,001
Hb loss or transfusion	8,8*10-8	1,29*10-8 – 6,11*10-7	<0,001
Redo surgery	3,27*10-8	4,85*10-9 – 2,2*10-7	<0,001

4. Discussion

The primary aim of this study was to evaluate the use of ARISTA™ AH as a topical haemostatic agent in MIS thoracic procedures and the impact on post operative morbidity and length of stay.

Intra and postoperative-blood loss are related with poorer outcomes in thoracic surgery and are responsible for unnecessary overall healthcare costs. Moreover, the requirement of blood products is associated with possible risks including adverse reactions and transfusion related injury [19]

Several haemostatic agents have been used in thoracic surgery and recently powders have been introduced. A RCT of 291 surgical patients treated in 9 centres in 3 surgical specialities (general, cardiac, and orthopaedic) showed the superiority of using ARISTA™ AH versus control. The study reported that 90.3% of patients treated with ARISTA™ AH achieved complete haemostasis within 5 minutes (only 3 minutes for cardiac) versus 80.4% in the control group ($p<0.0001$). Moreover,

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ARISTA™ AH showed a shorter time to haemostasis of the first treated lesion (1 minute versus 2 minutes for control; p=0.002) [20].

A retrospective analysis conducted by Bruckner et al on 240 patients undergoing complex cardiothoracic procedures (137 patients in the ARISTA™ AH group versus 103 patients in the control group), reported better short-term outcomes for the ARISTA™ AH group. Specifically, a significant decrease in haemostasis time (93.4+41 min in the ARISTA™ group versus 107.6+56 min in the control group; p=0.02), in chest tube output at 48 hours (1594+949 ml in the ARISTA™ group versus 2112+1437 ml in the control group; p<0.001), and lower transfusion requirement of blood products (2.4+2.5 units in the ARISTA™ group versus 4.0+5.1 units in the control group; p≤0.001) in the ARISTA™ group [21].

There are no data on routine used of ARISTA™ after MIS lung resection. In the present study we focused on intraoperative time, chest tube output, complications, reoperation and length of postoperative stay impact of ARISTA™ compared to the other haemostatic used in thoracic surgery. We reported that the cohort of patients treated with ARISTA™ had a significant reduction in total drain volume by 135 mls(standard error 53.9; p=0.012).

Moreover, the use of ARISTA™ significantly reduced the odds of post-operative complications, need for transfusion and redo-surgery.

Notwithstanding a countless range of topical absorbable haemostatic agents that are available for clinical use, limited clinical evidence exists comparing features (e.g. handily using, method of utilization, application time and storage requirements) and clinical effectiveness of those products. The great majority of our patients were intraoperatively treated with two different haemostatic agents with the same action: both ARISTA™ AH and SURGICEL are non-active, mechanical agents, used for minor to modest bleeding control.

ARISTA™ AH is a safe and effective, fast acting haemostat, useful in minimally invasive surgery to control minor bleeding after lymphadenectomy, especially in difficult areas (e.g. under recurrent laryngeal nerve) and for bothersome oozing along the stapler line (both for parenchymal and vessel stapler line) and it is very effective even when used alone. ARISTA™ AH is easy and ready to use, can be left in the haemostatic site due to the short absorption time without leaving any foreign body which can create false images that can be misinterpreted on CT-scan. Moreover, compared to other haemostats ARISTA™ AH showed significantly reduced the odds of post-operative complications, need for transfusion and redo surgery.

Furthermore, there is an assumed health economic benefit of ARISTA™ AH use, given the lower incidence of post-operative morbidity, less resources are spent on the patient pathway to recovery. Zaraca et al [22] leveraged this hypothesis in a randomised controlled trial setting exploring sealant use to reduce post-operative air leak. Indeed, sealants were significantly associated with less air leak and subsequently less morbidity which conferred obvious cost implications. Further investigation in the form a robust cost-effectiveness ratio (ICER) or cost-benefit analysis is warranted to explore this health economic impact. Aside from the economic benefit, incorporation of haemostat use into an ERAS pathway would serve to augment the patient journey and enhance time to recovery.

According to our results, the intraoperative use of ARISTA™ AH alone can be adequate for minor-modest bleeding control and can help to reduce costs related to postoperative bleeding, complications, prolonged in hospital stay and surgical time.

5. Limitations

The present study has several limitations. First of all is a retrospective study without the power of a randomized clinical trial. Moreover, the group of patients are not homogeneous in terms of number of treated patients' subjects. However, it is a large, two centres, study and after adjusting for possible confounding factors, we obtained comparable results.

6. Conclusions

While considering the limitations due to the retrospective nature of this study, we believe that a critical evaluation of a large cohort of patients can help to determine application and effectiveness of this agent in minimally invasive thoracic procedures.

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ARISTA™ AH is a safe and effective haemostat that can help surgeons to control modest to limited bleeding and oozing during surgical procedures with superior short-term outcomes of treated patients versus control.

Author Contributions: (I) Conception and design: SR, GC, AB, AJP, (II) Administrative support: GC, AB, (III) Provision of study materials or patients: FF, SV, DAF, (IV) Collection and assembly of data: SR, AJP, (V) Data analysis and interpretation: DAF, LP, AJP, SR, (VI) Manuscript writing: all authors, (VII) Final approval of manuscript: all authors.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.
Data Availability Statement: Suggested Data Availability Statements are available in section "MDPI Research Data Policies" at https://www.mdpi.com/ethics.

Conflicts of Interest: The authors declare no conflicts of interest.

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