REVIEW ARTICLE

Thromboembolic events from the intraoperative use of topical gelatin and albumin-glutaraldehyde haemostatic agents

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Abstract

Introduction

An under-recognised complication of gelatin-based [GBA] and albumin-glutaraldehyde-based haemostat agents [AGA] is their potential to embolise. This review aims to collate and analyse cases reported in the literature of perioperative thromboembolic phenomena secondary to locally applied GBA and AGA agents.

Methods

An electronic search was performed on databases Embase, Ovid Medline, Proquest, Scopus and Pubmed. 8875 articles were reviewed from title and abstract. After exclusion criteria and duplicates were removed, 13 articles with 18 cases were included for analysis. Data extracted from each of the articles included patient demographics, surgery type, the haemostatic agent used, clinical features, radiology and pathological findings, and associated morbidity and mortality.

Results

Thromboembolic events reported included fourteen secondaries to GBA and four from AGA. Cases included twelve pulmonary emboli, three peripheral emboli, two cerebral emboli and one coronary embolus. Embolic phenomena were most common following spinal orthopaedic surgery in GBA patients [43%], and Type A Aortic dissection repair in AGA patients [100%]. The application of 10ml or more of GBA was frequently reported in cases [64%]. Six cases were fatal. The time course of each event ranged from occurring intraoperatively to 45 days post-operation.

Conclusion

GBA and AGA agents are associated with venous and arterial embolisation and high overall mortality. GBA application over an unclear bleeding site poses a risk of arterial embolisation. Surgical fields should be dried before the application of AGA. Quantities of GBA > 10mL were frequently reported. GBA and AGA embolisation can occur anywhere from immediate to 45 days postoperatively.

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Introduction

Topical haemostatic agents are routinely used as an adjunct to promote haemostasis in a variety of surgical settings, and are considered a relatively safe class of agents [1, 2]. These agents are fundamental in reducing perioperative blood loss, which translates to reductions in blood transfusions, hypothermia, acidosis, length of hospital stay and mortality [3]. In our recent review, we highlighted the importance of recognising Gelatin based agents [GBA] in their potential to precipitate anaphylactic reactions [4]. Thromboembolic events across the spectrum of peripheral venous thrombosis, to venous and arterial embolism at various vascular beds are rare complications reported with mechanical and flowable gelatin based agents [GBA], as well as albumin-glutaraldehyde adhesives [AGA]. Literature regarding this complication is largely based on case reports across a variety of operations, but all similarly reporting a high mortality. We present a comprehensive review synthesising the literature relating to GBA and AGA agents. It will highlight the importance and awareness of considering this differential when these agents intraoperatively are used intraoperatively, provide pathophysiological mechanisms for agent propagation, and provide insight and elaborate on the perioperative diagnosis and management of this condition.

Materials and Methods

Search strategy

Databases searched included Embase, Ovid Medline, Proquest, Scopus and CINAHL. The final search was completed on the 20 June 2021. A research librarian within the authors institution assisted with conduction the search, using the prescribed search terms in Appendix 1.

After removal of duplicates 8875 articles were screened against title and abstract [Figure. 1]. Highly specific inclusion and exclusion criteria were set as to answer the specific subject of thromboembolic phenomena secondary to topical haemostatic agents. Most articles were excluded as they

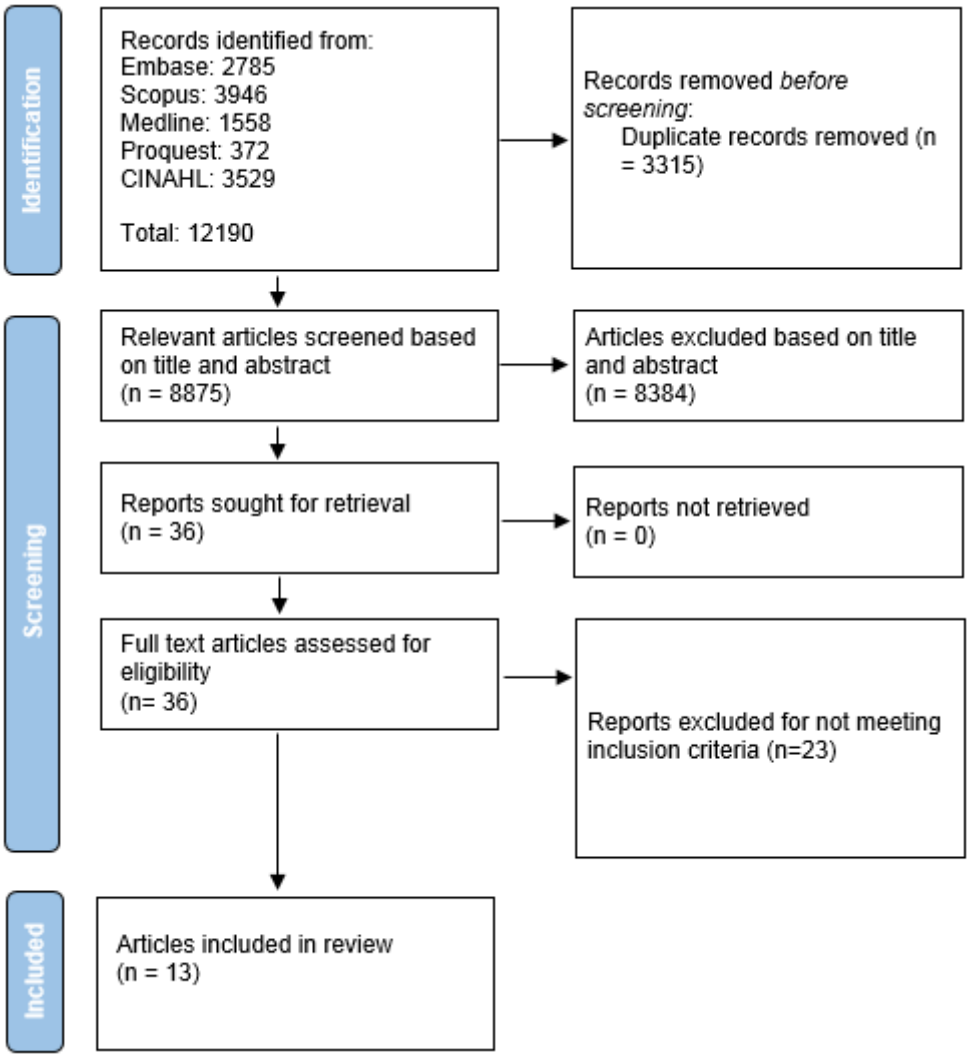

Figure 1. PRISMA diagram of selected articles

related to in-vitro or animal studies, or did not assess the outcome of interest of thromboembolic phenomena.

Study selection

We included case series and case reports describing intraoperative or postoperative thromboembolic phenomena deemed secondary to GBA or AGA agents. The bibliographies of included articles were analysed to increase the effectiveness of the literature search. Two authors independently reviewed the titles and abstracts. Studies or reports were included if they contained one of the outcome variables of interest: arterial or venous embolism secondary to GBA or AGA in any vascular bed including; extremity, gut, pulmonary, cardiac and cerebral. Articles must have described either the incidence, clinical manifestation, pathophysiology, diagnosis or management to be eligible. Studies or reports involving agents other than GBA and AGA, and those describing air, gas or fat embolism were excluded. Articles published in the non-English literature, letters, editorials, in-vitro or animal studies were excluded.

Data extraction

Patient demographics, surgery type, incidence rates, haemostatic agent used, clinical manifestations, location of thromboembolic event, differential diagnosis considered, pathology and imaging findings, case management and complications were drawn out.

Results

A total of 13 articles, including ten articles related to GBA and three related to AGA were retrieved [Table. 1].

Gelatin based haemostatic agents

Ten articles, comprised of eight case reports [5, 6, 7, 8, 9, 10, 11, 12] and two case series [13, 14] reported a total of 14 events attributable to the GBA used. Within case reports and case series, thromboembolic events reported included 12 pulmonary emboli and two cerebral events [13]. Patient ages ranged between 11 and 78 years. Five [35%] cases were fatal [8, 10, 11, 13]. Five cases were confirmed to be secondary to embolisation of the haemostatic agent through pathological

Table 1. Summary of literature for perioperative embolic phenomena secondary to Gelatin and Albumin-glutaraldehyde based agents.

Author	Methodology	Age	Surgery	Haemostat Used + volume	Intraoperative vs post-operative day	Signs/Symptoms	Radiology/Pathology	Embolic location	Complications	Mortality (Y/N)	Management
Ferschl et al. (2009)	Case report	18	Thirteen level spinal fusion	Surgifoam	Intraoperative	Hypotension and hypocapnea.	TOE: Increased right ventricular volume, reduced systolic function + leftward septal bowing + small left ventricle + numerous mobile masses migrating from right atrium to right ventricle	Right atrium + Right ventricle + segmental/subsegmental pulmonary arteries	Right heart failure + Cardiac arrest	N	CPR. Followed by low dose heparin infusion 3 months of therapeutic anticoagulation.
Wei et al. (2015)	Case report	68	L4-5 transforaminal lumbar interbody fusion	Surgifoam and recombinant thrombin + thrombin-soaked absorbable gelatin sponges	Post-operative day 3	Dyspnea and hypoxia	CTPA: Multiple bilateral segmental and subsegmental PE's	Pulmonary arteries	PE	N	Heparin infusion. Bridged to warfarin for 6 months.
Sagar et al. (2017)	Case report	38	L5/S1 discectomy	Thrombin based haemostatic matrix (not specified)	Post-operative day 5.	Left sided chest pain and dyspnoea	CTPA: heterogeneous filling defect with mixed attenuation + 'pseudoair pattern' in the left main pulmonary artery	Left main pulmonary artery	PE	N	Therapeutic heparin infusion. Switched to 6 months of Warfarin
Steinestel et al. (2012)	Case report	78	Removal L5 dorsal root ganglion schwannoma	FloSeal	8 hours post operatively	Dyspnoea and haemodynamic instability	CTPA: Numerous filling defects throughout both pulmonary arteries TTE: Transthoracic echocardiogram showed septal hypokinesia + paradoxical septal movement + marked dilatation of the right ventricle Pathology: Thin, peripheral rim containing erythrocytes and fibrin, with the rest of the thrombus consisting of acellular, eosinophilic granula with enclosed fibrin and thrombocytes. Identical to Floseal	Both main pulmonary arteries	Right Heart failure + Cardiac arrest	Y	CPR
Mura et al. (2018)	Case report	63	Laparoscopic Cholecystectomy	Floseal	Immediate post-operative	Dyspnoea, tachycardia, hypertension and hypoxia	CTPA: Multiple scattered bilateral minus images of the segmental and sub segmental branches of the pulmonary artery	Pulmonary arteries	PE	N	Conservative.
Ji et al. (2020)	Case report	11	Posterior spinal fusion	Gelatin sponges	Intraoperative	Hypotension, bradycardia, desaturation, and decreasing end-tidal carbon dioxide	TOE: hypokinetic and dilated right ventricle with severe tricuspid regurgitation and a D-shaped small left ventricle with normal function Pathology: Diffuse embolization of the pulmonary arterioles with amorphous, haemogenic, and blue foreign substances	Diffuse embolization of the pulmonary arterioles	Cardiac arrest	Y	CPR, followed by heparin bolus 0.5mg/kg
Skovrlj et al. (2014)	Case report	56	Multilevel lateral interbody fusions and thoracolumbosacral instrumented fusions with bilateral iliac fixation	Surgifoam	Intraoperative	Drop in the patient's recorded end tidal CO2 level, the reading from the arterial line became flat, and the patient lost his pulse	Pathology: angulated particles of embolic sealant with entrapped red blood cells within small-and-medium-sized vessels of the lungs and heart	Pulmonary arteries and coronary arteries	Cardiac arrest	Y	CPR
Bezanko et al. (2021)	Case report	33	Ultra-low anterior resection	Surgiflo	Intraoperative	Haemodynamic instability	CTPA – Bilateral segmental pulmonary emboli	Pulmonary arteries	PE	N	Nil
Coss et al. (2020)	Case series	1. 44 2. 63	1. Spinal fusion of C3 + peridontoid mass biopsy 2. Anterior cervical discectomy, bilateral foraminotamies + C3-6 vertebral fusion.	1. Gelfoam 2. Floseal	1. Immediate post-operative 2. Immediate post-operative	1. Right nystagmus and right arm dysmetria 2. Delayed awakening and was not breathing spontaneously	Pathology: 1. Occlusion of the right vertebral artery by red-gray material. foreign material morphologically consistent with Gelfoam. amorphous eosinophilic branching nonbirefringent foreign material 2.Thromboembolic occlusion by a red-gray material. Eosinophilic foreign material morphologically consistent with Floseal. Amorphous eosinophilic branching non-birefringent material	1. Right vertebral artery 2. Right vertebral artery + Right distal brachial artery, radial artery + ulnar artery.	1. Right lateral medullary infarct 2. Infract of pons, inferior left cerebellar hemisphere, vermis, and right frontal lob	1. Y 2. Y	1. Intra-arterial thrombolysis and thrombectomy with recanalization of the basilar and right vertebral arteries 2. Conservative

Yue et al. (2017)	Case series	1.66 2.74 3.72 4.63	1. WLE, right segmental mandibuletomy, partial maxillectomy and radial free forearm flap reconstruction 2. WLE, subsigmoid segmental mandibulectomy, partial maxillectomy, right neck dissection and anterolateral thigh free flap reconstruction 3. Left segmental mandibulectomy, subtotal glossectomy, radical excision left infratemporal fossa and fibula free flap reconstruction 4. Lateral mandibulectomy, subtotal glossectomy, neck dissection + free fibula reconstruction	Floseal	1.Day 4 post-operative 2.Day 3 post-operative 3.Day 17 post-operative 4.Day 6 post-operative	All: persistent tachycardia for more than 24 h, fever of more than 37.8C, and decreased oxygen saturation below 95%	CTPA: 1. Segmental branches in the right upper and middle lobes with a non-occlusive thrombus in the right lower lobar artery 2. Pulmonary emboli involving right upper, middle and lower lobe subsegmental arteries 3. Right middle lobe segmental pulmonary artery 4. Bilateral segmental and subsegmental pulmonary arteries	Pulmonary arteries	All: PE	All: N	Heparin infusion followed by warfarin for 6 months
Feghaly et al. (2011)	Case report	54	Bentall Procedure for type A Aortic Dissection	Bioglue	Day 45 post-operative	Cold, pain and paraesthesia in her right leg	Duplex US: Lower limb showed a complete occlusion of the right common iliac artery Pathology: Pathological analysis of those pieces revealed consolidated Bioglue.	Right common femora artery	Right leg ischemia	N	Arterial thrombectomy
Mahmood et al. (2004)	Case report	74	Type A Aortic Dissection repair	Bioglue	Day 6 post-operative	Chest pain, tachycardia, tachypnoea and hypotension	Pathology: Bioglue within left circumflex artery + right coronary + diagonal branch of LAD	Left circumflex artery, right coronary artery and the diagonal branch of the left anterior descending artery	Myocardial Infarction + Cardiac arrest	Y	CPR
Bernabeau et al. (2005)	Case report	1.30 2.76	1. Type A aortic dissection repair 2. Type A Aortic dissection repair	1. Bioglue 2. Bioglue	1. Day 14 post-operative 2. Intraoperative	1. Sudden short distance left limb claudication, with absence of left popliteal and posterior tibial and pedal pulses 2. Absence of previously patent radial pulse.	Pathology: 1. Bioglue on analysis. 2. Histopathologic examination of the embolic material confirmed it to be Bioglue	1. Popliteal artery 2. Humeral artery	1. Left lower limb ischemia 2. Upper limb ischemia (unclear which side)	Both: N	1. Embolectomy using Fogarty catheter. 2. Thromboembolectomy with Fogarty catheter.

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PE= Pulmonary embolism, WLE= Wide local excision, CTPA= Computed-tomography pulmonary angiogram, TTE= Transthoracic echocardiography, TOE= Transoesophageal echocardiography, US= ultrasound, CPR= Cardiopulmonary resuscitation.

analysis [8, 10, 11, 13]. The remaining cases were diagnosed on echocardiogram [5] or Computed Tomography Pulmonary Angiogram [CTPA] [6, 7, 14, 12]. Nine cases from case reports or case series reported using either >10ml of agent or 'a large number' gelatin sponges [5, 6, 10, 11, 8, 14]. One case reported using 5ml of Surgiflo[[12]. The remaining cases did not report the volume used. Intraoperative, or immediate post-operative events included six PE's [5, 8, 9, 10, 11, 12] and two cerebral events [13]. Of those PE's, 67% of patients rapidly deteriorated into cardiac arrest, with the remaining two patients developing haemodynamic instability. Products administered included; Gelfoam[[Pfizer, US] [13], Floseal[[Baxter, US] [8, 9, 13, 14], Surgifoam[[Ethicon, US] [5, 6, 11], Surgiflo[[Johnson & Johnson Wound Management, Somerville, NJ] [12], Thrombin-soaked absorbable gelatin sponges [Ethicon, US] [6], Gelatin sponges [Fukangsen, Guilin, China] [10].

Albumin-glutaraldehyde based haemostatic agents

Three articles reported a total four cases attributable to AGA use [15, 16, 17]. Thromboembolic events included three peripheral emboli and one cardiac embolus [15, 16, 17]. Ages ranged between 30-76. One case was fatal due to coronary embolism [16]. The sole agent used was Bioglue[[Cryolife Inc, Kennesaw, Ga] and the sole surgery was repair of type A aortic dissection. One case reported using 35ml [15], with the remaining cases not reporting volume used. All cases were definitively diagnosed on pathological analysis. One case of peripheral embolism was identified intraoperatively [17], the remaining were diagnosed post-operatively up to 45 days [15, 16].

Discussion

Herein we have summarised 18 published cases of embolism secondary to GBA and AGA agents. Strikingly there was an overall mortality of 33%, with immediate intraoperative hemodynamic compromise and cerebral embolisation a harbinger of mortality, with 67% and 100% of cases fatal, respectively. It is not clear if this reflects under recognition of GBA and AGA embolisation, lack of clear guidelines and/or no definitive treatment. Intraoperative haemodynamic compromise has numerous potential precipitants. This review and our previous work highlight two causes; pulmonary embolism and anaphylaxis as a cause after use of topical haemostatic agents [White et al. 2021]. The ability for a haemostat to embolise is not arbitrary and reflects its nature and intended use. GBA agents are composed of a granulated gelatin based matrix that may or may not be mixed with thrombin prior to administration [18]. Bioglue[is composed of purified bovine serum albumin [45%] and glutaraldehyde [10%]. These agents act at varying points in the formation of a clot, with the gelatin and AGA component swelling on application to provide a mechanical seal and the GBA thrombin component subsequently activating secondary haemostasis through the coagulation cascade [19]. We have categorised the discussion of embolisation in this review into arterial and venous. Note, albeit pulmonary emboli anatomically involve the pulmonary arteries, they are part of the venous thromboembolism spectrum and thus we are characterising these as venous emboli.

Arterial Embolisation

Overall, there were six cases of arterial embolisation with a mortality of 50% [17; 15, 13, 16]. In the absence of a patent foramen ovale, it is likely arterial embolisation originated from direct GBA application over an arterial vascular bed. Four patients suffered Bioglue[embolisation secondary to its usage in type A aortic dissection repair [15, 16, 17]. Bioglue[is a relatively watery and transparent adhesive, and its role in repair of type A dissection is a well-known quandary in cardiothoracic surgery [20]. It has been previously reported that the three likely mechanisms of Bioglue[embolisation include unintended spillage into true lumen, entry into the true lumen via escape through distal re-entry sites and leaking through anastomotic needle sites [21]. Furthermore, as blood perturbs the haemostatic mechanism and bonding of Bioglue[to aortic tissue, the lumen should be appropriately dried before its application otherwise this may pose a risk of embolisation [22]. One of the four cases was associated with mortality, with the single case having unique embolisation into the coronary vasculature [16]. It is suggested to prevent Bioglue[embolisation into the coronary ostia, a moist sponge can be placed in the true lumen during application of Bioglue[[22]

Two cases of cervical neck surgery led to vertebral artery occlusion and subsequent cerebral infarction. In this case authors identify brisk and heavy bleeding of unclear origin which they applied Gelfoam[and Floseal[to with subsequent haemostasis. It was not identified if the bleeding was arterial or venous. In cervical neck surgery the limited space combined with complex anatomy and magnification can result in an obscured field of view, which can be compounded with bleeding. Surgeons can lose sight, with some suggesting they blindly apply GBA [23]. This can lead to application and entrainment of GBA into an arterial bleed if the site is not identified. These cases highlight the critical importance of maintaining a dry surgical field during its use and ensuring direct vision when applying the agent. If there is concern for embolism, the wound can be flooded with saline to entrain this rather than apply further GBA.

Venous Embolisation

The second group of emboli were those that migrated through the venous system, most often centrally to the pulmonary vasculature. Six cases involved spinal surgery [5, 6, 7, 8, 10,

11] four head and neck reconstructions [14]. one cholecystectomy [9], and one ultra-low anterior resection [12]

Embolisation to the pulmonary vasculature from the spinal venous network is complex and dependent on location of surgery and application of GBA. The vertebral venous plexus is comprised of the internal plexus, external plexus and the horizontal basivertebral veins which drain into extraspinal veins centrally to the right atrium. The lumbar and thoracic vertebral plexus drains into the azygous venous system, and the cervical regions empties into the vertebral and jugular veins. However, the surgeon need be aware that the venous spinal system is valveless and interconnected, lending itself dependent on gravity, thoracic and abdominal pressures, and patient positioning. It is well known in spinal surgery that patient positioning is implicated in thromboembolism, with reported incidence as high as 12% [24], and likely reflects the valveless nature of this system. The positioning of a patient is surgeons' preference, however positioning of the patient will affect venous pressures and risk of bleeding vs. embolism. Risk of embolism or GBA entrainment is higher if there are low venous pressures [surgical site elevated above the heart], whereas risk of bleeding is higher with higher venous pressures [surgical site below the heart] [25]. We suggest if there is suspicion of GBA embolism, the tilt of the operating table can be adjusted to reduce the negative pressure gradient between the site of operation and the right atrium.

Head and neck surgery may be associated with propagation to the pulmonary vasculature due to exposure of the pterygoid plexus, a venous network with a large endolumen, which may allow the propagation of foreign material through its channels via the retromandibular and external jugular veins to the pulmonary arteries. Of note, the pulmonary emboli which occurred secondary to GBA application to the pterygoid plexus occurred between 3 – 30 days post operatively, which may reflect the lateral pterygoids association to the pterygoid plexus. The lateral pterygoid exerts an effect on the pterygoid plexus during its contraction, creating a pump like effect which propagates blood back to the heart, however this may facilitate and dislodge GBA [26].

Whilst site of application is evidently important, volume used appeared to be a risk factor for subsequent embolisation. The finding that most cases GBA emboli were following application of > 10mL is consistent with previous work [5, 6, 8, 10, 11, 14]. Two retrospective cohort studies [27, 28] identified use of > 10ml as a risk factor for developing subsequent embolism – either DVT or PE, which is supported by the observation that both Floseal[and Surgiflo[may pass through 40um filters, far smaller than vessel lumens [29]. A multivariate analysis of embolic events in patients post meningioma surgery demonstrated 11 of the 12 patients who experienced embolic phenomena were administered at least 10ml of Floseal[[27]. Of note, prophylactic enoxaparin did not reduce the risk of thromboembolic events, supporting the case that these emboli were secondary to GBA material. These findings were replicated in Gazzeri et al's [2018] review of patients undergoing intracranial tumour surgery, with injection of 10ml or more GBA agent significantly increasing the risk of PE from 5.6% to 6.8% [p=0.02]. Whilst volume of these agents administered cannot always be helped, it is important to recognise this volume as a risk factor and monitor the patient closely for embolic phenomena post-operatively.

The overall incidence of these events is not determined, and likely under-reported. However, observational studies in patients undergoing meningioma and brain tumour resection found the embolic incidence to be 2.6% and 5.6%, respectively [27, 28]. Although there are relatively low case numbers, the presentation of intraoperative or immediate post-operative pulmonary embolism frequently cardiac arrest [67%], carrying a relatively high mortality of [75%]. This stands out from the reported mortality of up to 30% in 'massive' PE's from activation of the coagulation cascade [30]. The exact reason for this increased mortality is unclear, although, may be posited to there being no physiological lytic counter to GBA agents, as there is for a regular biological clot. Further, there have been several reports of GBA agents causing intractable bleeding through the development of bovine-associated antibodies cross reacting and depleting coagulation factors [31]. No study in this review reported measuring such antibodies, but speculatively the depletion of coagulation factors and subsequent bleeding could result in a depletion of any anti-thrombotic enzymes that would reduce the peri-GBA material clot burden.

The high percentage of patients who presented as rapidly deteriorating from a haemodynamic perspective underscores the importance of anaesthetic and surgical staff considering embolisation of GBA material. Although critical to consider and recognise intraoperatively, consideration must be given to GBA embolisation weeks following the agent administration. GBA and AGA agents can take between 4-6 weeks to fully reabsorb, and can present anywhere along this timeframe, as demonstrated by the numerous cases days or even weeks' post application [6, 14, 15, 16, 17, 27, 28].

Radiological Features

Echocardiography was utilised in 80% of intraoperative PE's, each demonstrating evidence of either thrombus migration or right heart strain [5, 8, 10, 12]. Postoperatively, CT was

successfully utilised to identify GBA emboli. Wei et al. [2015] described hypodensities [HU -100] in the pulmonary artery or venous sinus that, on first inspection, were consistent with intravascular air. Hypodensities on postoperative CT at sites of GBA use for liver resection [32], cervical surgery [13] and discectomy [7] have similarly been reported in the literature. This phenomenon, known as the 'pseudo-air sign' was first described by Learned et al. [2014] in patients following intracranial neurosurgical procedures. The mechanism of this finding can be understood through recognising GBA agents often incorporate a significant amount of air when deployed. On imaging this manifests as a low density in Hounsfield units, and is distinguishable from acute clot which tends to be hyperdense. No imaging characteristics were described for Bioglue[.

Histological Features

Macroscopically at autopsy, Gelfoam[and Floseal[embolism appeared as red-gray material [13] whereas Gelatin sponges appeared as amorphous, hemogenic, and blue foreign substances [10]. Histology of Gelfoam[and Floseal[demonstrated amorphous, eosinophilic, branching non-birefringent foreign material [13]. Steinstel et al. [2013] identified Floseal[as an embolus with a thin peripheral rim
10.4038/SLJS.V40I1.8924 erythrocytes and fibrin, with the rest of the thrombus consisting of acellular, eosinophilic granula with enclosed fibrin and thrombocytes. Skorvlj et al [2014] described Surgifoam[as angulated particles of embolic sealant with entrapped red blood cells. These histopathological findings can be understood through the 'foreign body reaction', which involves the immune system acting to 'wall off' non-degradable foreign bodies, with eosinophilic infiltrates representing the tendency for GBA agents to produce IgE mediated immune reactions [34].

Management

In cases with haemodynamic compromise, haemodynamic and life supporting measures should be instituted with no specific adjustment to the Advanced Life Support algorithm identified in any of the cases. In cases without haemodynamic compromise, GBA agents can take between 4-6 weeks to fully reabsorb, and monitoring for this complication should occur in the immediate post-operative period and follow-up reviews. A successful anticoagulation regime identified involved the commencement of a heparin infusion [5, 6, 14], until bridging to therapeutic Warfarin for a 3-6-month course [5, 6, 14], however this is low quality evidence. No case assessed the use of direct oral anticoagulants in the treatment of this condition.

Regarding interventional approaches, one case of vertebral artery embolism attempted intra-arterial thrombolysis and thrombectomy with recanalization which resulted in acute infarcts of the pons, inferior left cerebellar hemisphere, vermis, and right frontal lobe [13]. Although interventional thrombectomy was unsuccessful for GBA cerebral embolism, endovascular thrombectomy or embolectomy was effective in the treatment of all AGA peripheral emboli [15, 17]. This identifies a gap in the literature regarding the management of haemostat embolisation, and the measures utilised to manage it will require further assessment.

Implications and Take Home Messages

This review supplements the surgical literature on haemostatic agents, demonstrating their risk of embolism. Surgical site and volume of agent appear to be the predominant risk factors in the subsequent development of arterial and venous emboli. Intraoperative cardiovascular collapse after administration of AGA or GBA should alert the surgeon and anaesthetist to provide life supporting measures and reduce the negative gradient between the surgical site and right atrium. Communication at the time of GBA or AGA application, similar to the practice seen on injection of patent blue or bone cement, would assist in prompting anaesthetic staff to monitor for any haemodynamic compromise. Echocardiography is a useful tool in detecting GBA PE's intraoperatively, and intravascular hypodense material on computed tomography may assist the clinician with diagnosis of GBA post-operative setting. It is important to obtain a clear, dry field when using Bioglue[for Aortic surgery, and ensure all haemostatic agents are injected under vision.

1. Intraoperative haemodynamic compromise secondary to GBA embolism is associated with high mortality.
2. Haemostat application over an unclear source of bleeding, or into an oozy field site poses a risk of arterial embolisation.
3. Quantities of GBA > 10mL are significantly associated with thromboembolism.
4. GBA haemostat emboli may appear hypodense on CT imaging, and is reported to be due to the concomitant entrainment of air leading to a “pseudoair” sign.
5. GBA and AAG embolisation can occur anywhere from immediate to 45 days post operatively.

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APPENDIX 1: SEARCH TERMS

[surgiflo OR gelfoam OR floseal OR surgifoam OR haemostat* OR hemostat* OR gelatin OR 'gelatin sponge' OR "albumin with glutaraldehyde" OR "albumin-glutaraldehyde" OR "albumin glutaraldehyde" OR BioGlu*] AND [embol* OR thrombo* OR thromboemboli* OR infarc* OR "pulmonary embol*" OR "pulmonary infarc*" OR "cerebral embol*" OR "peripheral embol*" OR "cardiac embol*"] AND [topical OR local]

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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