Journal of Clinical Neuroscience 120 (2024) 30–35

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.journals.elsevier.com/journal-of-clinical-neuroscience

Expert panel recommendations for topical hemostatic agent use in varied bleeding sites and situations during neuro-spine surgeries

C.E. Deopujari [a], S. Ambekar [b], B.R. Yetukuri [c], B. Diyora [d], A. Ghosh [e], P. Krishnan [f], M. Panigrahi [g], R. Ranjan [h], C. Raman [i], S. Tyagi [j], S. Vaishya [k], N. Venkataramana [l], V.D. Sinha [m], D. Paniker [n], S. Das [o,*]

[a] Department of Neurosurgery, Bombay Hospital Institute of Medical Sciences, Mumbai, India
[b] Department of Neurosurgery, Jaslok Hospital, Mumbai, India
[c] Department of Neurosurgery and Spine Surgery, Yashoda Hospitals, Hyderabad, India
[d] Department of Neurosurgery, Lokmanya Tilak Municipal General Hospital and Lokmanya Tilak Municipal Medical College, Mumbai, India
[e] Department of Neurosurgery, Institute of Neurosciences Kolkata, Kolkata, India
[f] Department of Neurosurgery, National Neurosciences Centre Calcutta, Kolkata, India
[g] Department of Neurosurgery, Krishna Institute of Medical Sciences, Hyderabad, India
[h] Department of Neurosurgery, Aditya Birla Memorial Hospital, Pune, India
[i] Department of Neurosurgery, Nobel Hospital, Pune, India
[j] Department of Neurosurgery, Indraprastha Apollo Hospital, New Delhi, India
[k] Department of Neurosurgery, Fortis Memorial Research Institute, Gurugram, India
[l] Department of Neurosurgery, Brains Hospital, Bengaluru, India
[m] Department of Neurosurgery, Santokba Durlabhji Memorial Hospital, Jaipur, India
[n] Department of Neurosurgery, Aster Medcity, Kochi, India
[o] Johnson and Johnson Private Limited, Mumbai, India

ARTICLE INFO

Keywords:
Neuro-spine surgery
Intraoperative bleeding
Hemostasis
Topical hemostatic agents
Bleeding sites and situations
ORC
Flowable gelatin

ABSTRACT

Intraoperative bleeding poses a substantial challenge, particularly in neuro-spine surgeries leading to complications such as hematomas, infections, and hemodynamic instability. Despite their proven efficacy, use of topical hemostatic agents (THAs) lacks comprehensive published literature and guidelines particularly in the Indian setting. The present study provides the first-ever Indian expert panel recommendations for effective adjunct THA use in different intraoperative bleeding sites and situations in neuro-spine surgeries. A comprehensive approach, encompassing a literature review, followed by experience sharing in a meeting using a survey helped integrate expert opinions in the form of practical algorithms to guide THA selection. Our survey results revealed a strong inclination towards specific THAs, flowable gelatin + thrombin being choice of THA for difficult to access and problematic bleeding situations during tumor removal/resection, transsphenoidal hypophysectomy and skull-based procedures. Both oxidized regenerated cellulose (ORC)/Fibrillar and flowable gelatin + thrombin were recommended for continuous oozing. ORC/Fibrillar was preferred for arteriovenous and cavernous malformations. This expert-panel guidance on THA use aims to optimize hemostat use practices and improve surgical outcomes in neuro-spine surgery.

1. Introduction

Intraoperative bleeding remains a major complication in surgical procedures and bleeding complications arise in nearly 30 % of surgeries [1,2]. Neuro-spine surgery, in particular, has unique challenges due to the potential for significant intraoperative blood loss from large wound surfaces and cancellous bone. This results in long operative hours, elevates risk of postoperative complications such as hematomas and infections, and may even cause hemodynamic instability [3–5]. The impact of intraoperative bleeding extends beyond the immediate surgical setting. The need for blood transfusions, prolonged stays in intensive care units, and ventilatory support often contribute to longer

* Corresponding author at: Arena Space, behind Majas Depot, Shyam Nagar, Jogeshwari East, Mumbai, Maharashtra 400060, India.
E-mail address: SDas186@ITS.JNJ.com (S. Das).

https://doi.org/10.1016/j.jocn.2023.12.007
Received 11 October 2023; Accepted 11 December 2023
Available online 3 January 2024

recovery times and a greater economic burden [3–6]. Therefore, it is crucial to identify effective and safe strategies to minimize intra-operative bleeding during neuro-spine surgery, to enhance surgical outcomes and patient safety.

Various approaches are available for achieving hemostasis including mechanical methods, pharmacologic agents, and topical hemostatic agents (THAs) [5]. THAs can be classified into different categories based on their properties and mechanisms of action, such as mechanical, active, flowable, and fibrin sealants [7]. These agents, act as mechanical barriers, promote platelet aggregation, trigger coagulation, and seal surfaces [8]. Their clinical use has shown promising results, leading to shorter operating hours, reduced transfusion requirements, and shorter hospital stays [9–11].

Despite the proven efficacy of THAs, their use in neuro-spine surgery lacks comprehensive published literature and specific guidelines, particularly in the Indian setting. While existing recommendations from the 2022 Spine Expert panel and the American Society of Anesthesiologists emphasize the importance of multimodal protocols, there is a notable absence of specific algorithms for the utilization of THAs [12,13]. This highlights the critical need for a guidance document that guides the selection and application of THAs in neuro-spine surgery, considering the specific properties of THAs, bleeding situations, and surgical procedures.

To address this need, the expert panel, consisting of leading opinion leaders in the field, has developed the first-ever Indian expert panel recommendations. These recommendations offer a practical and targeted approach to the use of THAs in the Indian setting. They also provide guidance on the use of THAs in neuro-spine surgery, aiming to optimize hemostatic practices, improve surgical outcomes, and enhance patient safety.

2. Methodology

We performed a narrative literature review on intraoperative bleeding incidence, challenges, and different hemostatic methods used in neuro-spine surgery. The literature search included relevant randomized controlled trials, review articles, meta-analyses, and available guidelines on the management of intraoperative bleeding in neuro-spine surgery and the use of THA. We used PubMed search database with the relevant keywords like “hemostats,” “surgical bleeding,” “bleeding”, “hemorrhage,” “hemostatic agents,” “surgical hemostats,” “blood loss,” “spine surgery,” “neurosurgery,” “neuro-spine surgery,” “hemostasis,” “topical hemostats,” “THA,” “intra-operative bleeding,” “perioperative bleeding,” “impaired hemostasis in surgical patients,” “bleeding in neurosurgery,” “bleeding in spinal surgery,” “critical challenges in surgery,” “blood loss in neurosurgery,” “blood loss in spinal surgery,” “impact of bleeding,” “bleeding-related complications in surgeries,” “use of hemostat in surgery,” “use of topical hemostat in surgery,” “use of topical adjunctive hemostat in spine/neurosurgery,” “role of hemostat agent in surgery,” “management of blood loss with hemostat,” “recommendations for topical hemostats,” “consensus statements on use of topical hemostats,” “use of hemostats,” “hemostats for spine surgery,” “hemostats for neurosurgery,” “perioperative blood loss,” “perioperative bleeding management,” “intraoperative bleeding management” “bleeding management in surgeries.”.

A literature review document was developed, shared with, and analyzed by an expert panel of 15 neuro-spine surgeons from across India, 10 days before the face-to-face advisory board meeting (ABM). The ABM held on 25th March 2023 in Mumbai was attended by 13 experts. The advisory board captured the clinical experience of the experts in various bleeding scenarios pertaining to the use of THA. A survey-based approach was employed, and two questionnaires were circulated to collect and integrate expert opinions on intraoperative bleeding incidence, complications, impact, and choice of topical hemostat for

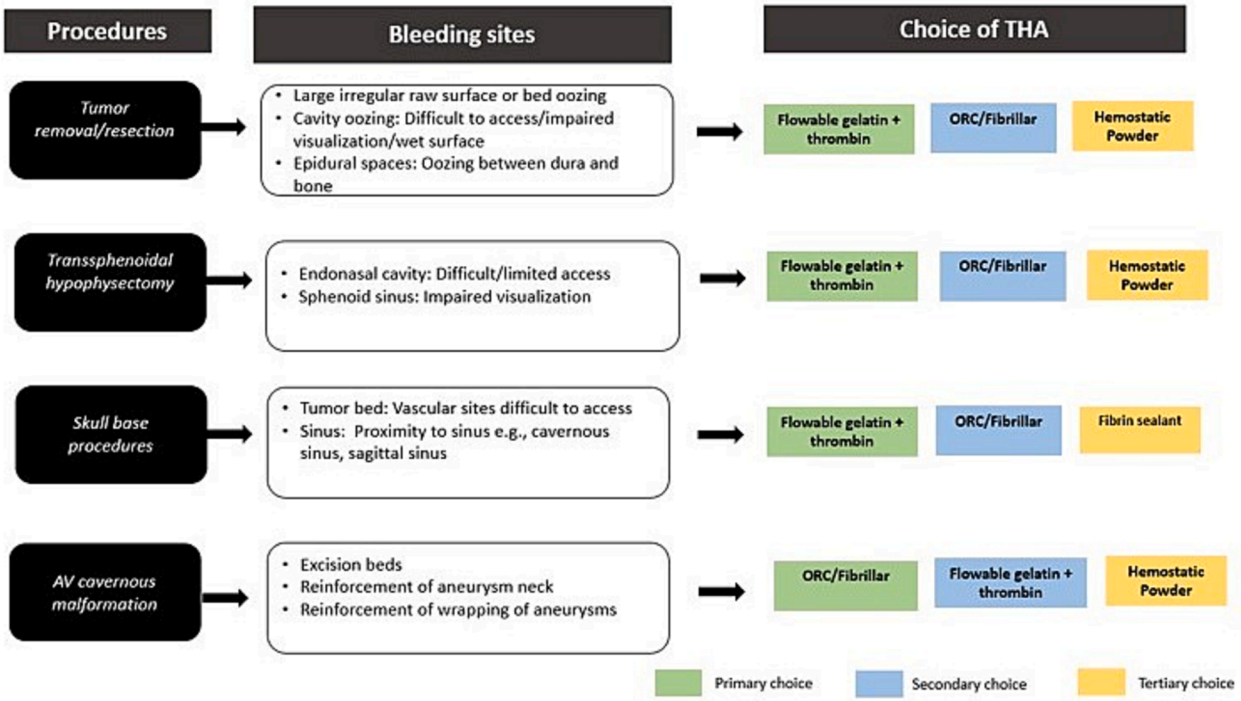

Fig. 1. Recommended THA for different bleeding sites & situations in different procedures, THA: Topical: hemostat; ORC: Oxidized regenerated cellulose; AV: Arteriovenous.
The figure outlines the selection of THAs based on specific criteria, such as the nature of bleeding, access difficulties, visualization, and proximity to critical structures, for each procedure listed. It also indicates the primary, secondary, and tertiary choices of THAs in different bleeding sites and situations in each of the procedures.

different bleeding sites, situations, and procedures (Fig. 1).

The results of both survey rounds were analyzed and discussed by the experts. The final algorithms were generated by way of a combination of evidence from literature, experience sharing, survey results, and recommendations suggested by the expert panel.

3. Results

3.1. Intraoperative bleeding in neuro-spine surgery and its impact on patient outcomes:

In the survey, with regards to intraoperative bleeding, 45.4 % of the surgeons agreed that they observed at least 10 % incidence while 9.1 % reported a higher incidence of up to 30 %. The majority (90 %) concurred that intra-operative bleeding leads to complications impacting patient outcomes, and resource utilization. The cost of hemostats is a factor to consider and 90 % of the experts agreed that THAs are cost-effective and reduce complications.

3.2. Agreement on the intraoperative bleeding scale in neuro-spine practice

The intraoperative bleeding scale's grades are based on the visual field, anatomic appearance, qualitative description, and visually estimated blood loss. According to this scale, the visually estimated rate of blood loss is categorized as follows: mild bleeding: >1.0–5.0 mL/min, moderate bleeding: >5.0–10.0 mL/min severe bleeding: >10.0–50.0 mL/min and life-threatening bleeding: >50.0 mL/min [14,15]. More than half (54.5 %) of the experts concurred with the Intraoperative bleeding scale – validated intraoperative bleeding scale (VIBe scale).

3.3. Recommended use of THA in different neuro-spine procedures and bleeding sites

In the survey, most of the expert's first preferred and recommended choice of THA was flowable gelatin plus thrombin for tumor removal or resection, transsphenoidal hypophysectomy, skull base procedures, and venous plexus followed by oxidized regenerated cellulose (ORC)/Fibrillar for arteriovenous malformations (AVM) and cavernous malformations. The experts emphasized that hemostatic agents should be selected based on the individual case situation and rated their choice of hemostat accordingly.

The percentages in Table 1 represent experts' responses to Questionnaire 1. Experts opined that among the different neuro-spine bleeding situations, the choice of THA varied based on the specific procedure and the bleeding. For tumor removal or resection procedures, particularly those involving large raw surface or bed oozing, cavity oozing, or epidural spaces bleeding sites, the majority (73.3 %) of the expert panel members recommended the use of flowable gelatin + thrombin.

Thus, opinions about the choice of THA for different neuro-spine bleeding situations varied among the expert panel members, reflecting the complexity of the procedures and the need for tailored approaches. Additionally, the findings suggest that flowable gelatin + thrombin was a frequently preferred THA for a range of neuro-spine procedures. However, ORC/Fibrillar was the preferred choice for procedures like AVM and cavernous malformation.

3.4. Recommended THA as per bleeding situations in the neuro-spine segment

In the survey, experts agreed that ORC/Fibrillar and flowable gelatin + thrombin was the preferred choice of hemostat considering different neuro-spine bleeding situations such as continuous oozing from a broad surface, bleeding from difficult-to-access areas, and bleeding significantly impeding the progress of surgery (problematic bleeding). The percentages in Table 2 represent experts' responses to Questionnaire 2. It indicates the proportion of expert panel members who recommended each THA for the respective bleeding situation. Most of the experts (72.7 %) preferred ORC/Fibrillar for continuous oozing. On the other hand, flowable gelatin + thrombin was the THA of choice for difficult-to-access bleeding and problematic bleeding situations. Overall, the responses suggested that the choice of THA may vary depending on the bleeding situation and its severity.

Based on the expert opinion of neuro-spine surgeons across Indian regions during ABM, we present recommendations for consideration while selecting a THA (Figs. 1 and 2).

In addition to the survey results, the experts recommended certain key points (Table 3).

Table 1
Expert panel's preferred choice of THA for different neuro-spine procedures and bleeding sites.

Procedure	THA	N (%)
Tumor removal or resection	Flowable gelatin + thrombin	73.3
• Large irregular raw surface or bed oozing	ORC/Fibrillar	46.6
• Cavity oozing	Hemostatic powder	20.0
• Epidural spaces		
Transsphenoidal Hypophysectomy	Flowable gelatin + thrombin	80.0
• Endonasal Cavity	ORC/Fibrillar	26.7
• Sphenoid sinus	Hemostatic powder	6.7
Skull Base Procedures	Flowable gelatin + thrombin	80.0
• Tumor bed	ORC/Fibrillar	60.0
• Sinus	Fibrin sealant	40.0
	Others	6.6
AVM & Cavernous Malformation	ORC/Fibrillar	66.7
	Flowable gelatin + thrombin	33.3
• Excision bed		
• Reinforcement of aneurysm neck	Hemostatic powder	6.7
• Reinforcement of wrapping of 'Aneurysm'	Others	6.7

N: Number of experts (%). Response percentages in the table may not add up to 100% in some instances as surgeons were allowed to select multiple THA options. THA, Topical hemostatic agent; ORC, Oxidized regenerated cellulose; AVM, Arteriovenous malformation

4. Discussion

Our expert panel members agreed that intraoperative bleeding in

Table 2
Expert panel's preferred choice of THA for different bleeding situations in neuro-spine procedures.

Bleeding situations					
Continuous Oozing		Difficult to Access Bleeding		Problematic Bleeding	
THA	N (%)	THA	N (%)	THA	N (%)
ORC/Fibrillar	72.7	Flowable gelatin + thrombin	90.9	Flowable gelatin + thrombin	72.72
Flowable gelatin + thrombin	72.72	ORC/Fibrillar	27.27	Hemostat patch	54.54
Hemostatic Powder	27.27	Fibrin sealant	18.18	Fibrin sealant	27.27
		Gelatin sponge	9.09		

N: Number of experts (%). Response percentages in both tables may not add up to 100% in some instances as surgeons were allowed to select multiple THA options. THA, Topical hemostatic agent; ORC, Oxidized regenerated cellulose.

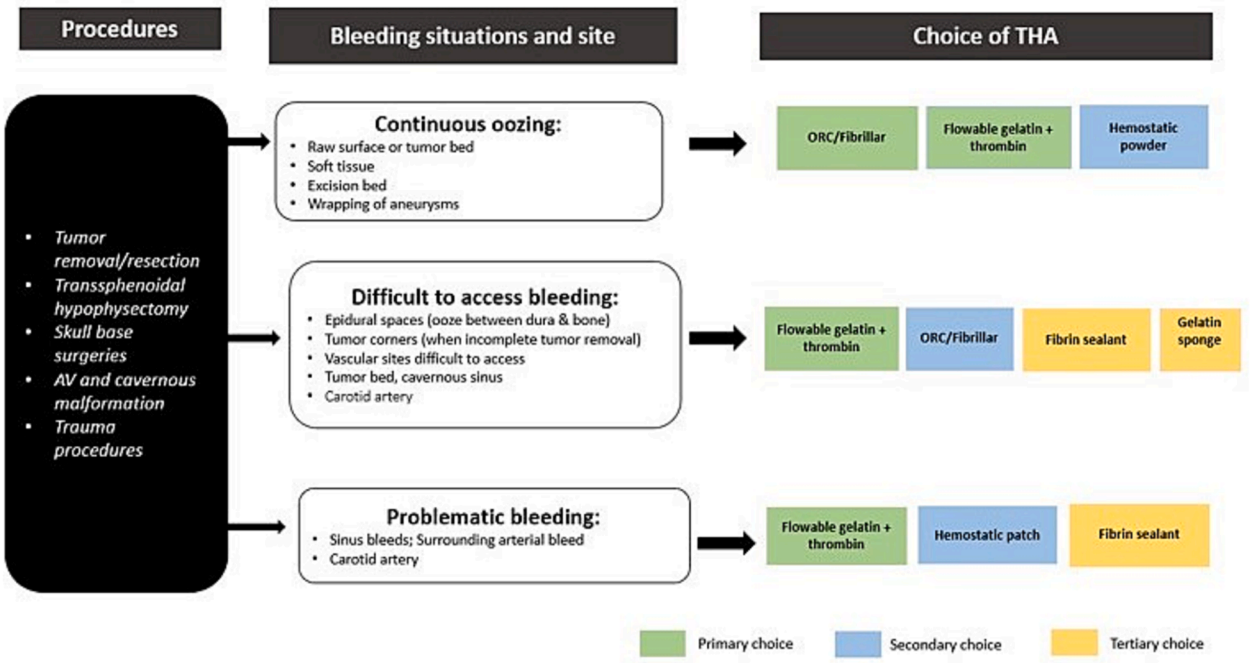

Fig. 2. Recommended THA for different bleeding situations*, *The effective use of al topical hemostats is contingent upon their proper application. Surgeons must undergo appropriate training to employ the correct techniques for optical outcomes. Topical absorbable hemostats are used adjunctively in surgical procedures to assist in the control of intra-operative bleeding when ligation or other conventional methods of control are impractical orineffective. THA: Topical hemostat agent; ORC: Oxidized regenerated cellulose; AV: Arteriovenous.
This figure guides on the selection of THAs tailored to specific bleeding situations encountered in a range of surgical procedures. Each surgical scenario is categorized based on the nature of bleeding, and the figure outlines the primary, secondary, and tertiary choices of THAs to achieve effective hemostasis.

Table 3
Additional recommendations.

The use of a pre-operative checklist that includes assessments such as bleeding and clotting time, prothrombin time, activated partial thromboplastin time, platelet count and optimization of the same can help prevent intraoperative bleeding complications.
Adequate training, referring to the user manual, or following the instructions for use to ensure proper utilization of these agents.
In cases of small sinus region and transforaminal percutaneous endoscopic lumbar discectomy, using ORC first in the proximal segment and then deeper sections, along with absorbable gelatin powder, can provide mechanical pressure and control bleeding.
Flowable gelatin is preferred for hemostasis in cavernous sinus tumor hemorrhage cases.
For skull-based tumor procedures, ORC combined with flowable gelatin and pressure is generally successful, but its suitability may vary depending on the specific skull-based bleeding circumstances.
Transsphenoidal pituitary surgery benefits from the use of ORC to stop diffuse oozing, while flowable gelatin is recommended for managing brisk bleeding near the carotid in pituitary adenoma cases.
The combination of thrombin and gelatin can be employed to control diffuse oozing following hematoma evacuation after glioma resection.
Oxidized regenerated cellulose can effectively manage profuse bleeding and venous ooze in various situations.

ORC: Oxidized regenerated cellulose.

neuro-spine surgery remains a critical challenge, worsening patient outcomes and ballooning healthcare costs, which was agreed upon by ABM members [6,16]. The current consensus is consistent with Neveleff's [5] study findings, which linked the impact of intraoperative bleeding (such as anemia, hypoxia, etc.) with higher costs [5].

Several THAs are available and are clinically proven for their use in neuro-spine surgery, including ORC, flowable gelatin with thrombin, hemostatic powders, absorbable gelatin sponge and fibrin sealants. Oxidized regenerated cellulose acts as a matrix for clot formation and stabilization by promoting the binding of hemoglobin to its oxycellulose structure. It swells upon absorbing blood, exerting mechanical pressure to control hemorrhage and activates coagulation on collagen surfaces. The low pH of ORC imparts antibacterial properties but should be applied judiciously to prevent tissue inflammation. It gets absorbed in 7–14 days [17,18]. Flowable gelatin + thrombin fills the bleeding site and swells to create a stable clot that conforms to wound contours. This clot formation also triggers platelet activation, further enhancing hemostasis. In addition, the thrombin component converts fibrinogen into a fibrin polymer, promoting fibrin formation in the coagulation cascade. It gradually gets absorbed over 6–8 weeks without any residue [19]. Hemostatic powder selectively targets bleeding areas, forms a physical barrier, and concentrates clotting factors, offering minimally invasive hemostasis [20]. Fibrin sealant acts by blocking holes in blood vessels to prevent leakage it gets absorbed in 10–14 days [21]. Gelatin sponge helps control oozing by forming a bulky artificial clot in vascular areas and gradually getting absorbed over 4–6 weeks [22].

As per our survey results, flowable gelatin with thrombin was the most recommended THA (Fig. 1). However, experts preferred ORC/Fibrillar across different neurosurgical procedures due to economic constraints and discussed that cost is an important factor to consider when selecting a medical intervention. Whilst ORC is not the lowest-cost hemostat available for use in surgery, it may represent the optimal choice in specific situations depending on the utility, efficacy, and potential avoidance of costly complications.

Franceschini et al. [23] reported ORC as a prominent topical hemostat utilized efficiently in neuro-spine surgery. This could be due to its ease of use, favorable bioabsorption, and biocompatibility [23]. In a clinical study conducted by Lei et al. patients ($n = 60$) undergoing cranial neurosurgery reported that ORC had a faster hemostatic effect and a significant hemostatic success rate ($p < 0.05$) versus gelatin sponge [24]. In situations, when ORC and other hemostatic agents were inefficient or inadequate to manage bleeding in the spinal epidural region, flowable gelatin + thrombin was found to be a useful hemostatic agent [25]. In another study, 31 patients who underwent craniotomy

were treated with flowable gelatin + thrombin for immediate hemostasis [26]. These findings are consistent with our survey results on using flowable gelatin + thrombin as the preferred hemostatic agent for skull base surgeries. Oxidized regenerated cellulose has also been shown to be effective in achieving hemostasis in patients with bleeding disorders, which may be particularly important in neuro-spine surgeries where bleeding is difficult to control [27].

Prabhu et al. [28] reported similar hemostatic effects between ORC and absorbable gelatin by substituting ORC with customized absorbable gelatin for lining the surgical cavities after excising brain lesions [29]. Despite being absorbable, ORC has also been linked to postoperative complications such as dural sac compression produced by hemostat masses [30]. These study findings were corroborated throughout the panel discussion, wherein the experts emphasized the importance of removing local hemostatic agents before closure to avoid any potential issues. Experts also emphasized the importance of acquiring knowledge and understanding the correct usage of hemostats.

Oxidized regenerated cellulose can be particularly useful in cases where electrocautery may impede visualization, as in bleeding during surgery on the pituitary via a transsphenoidal approach. Bleeding situations like mild persistent oozing from brain tissue following excision can be effectively addressed by using ORC prior to closure after removal [30]. These findings were consistent and aligned with our expert opinion of ORC/Fibrillar being the preferred option for bleeding situations such as continuous oozing. The expert panel also preferred flowable gelatin + thrombin for difficult-to-access bleeding and problematic bleeding situations.

Currently, due to the absence of Indian guidelines on the use of appropriate THA in various bleeding sites and situations in the neuro-spine segment, the current algorithms can be used as guiding document for in-clinic practice, especially by young surgeons. (Figs. 1 and 2). To our best knowledge, these algorithms are the first of their kind developed in the Indian context and provide a systematic approach in selecting appropriate THA based on the nature of the procedure and bleeding site, situations, and properties of THA.

Clinicians can make informed decisions and improve patient outcomes using the proposed algorithms. These algorithms are not intended to be prescriptive and should only be used as a general guideline for THA selection. Surgeons should make the final THA choice based on their clinical experience, patients' individual risk factors, and the specific details of the surgical procedure.

A limitation of our study was that the current algorithms were developed with only one round of surveys on the usage of different THAs. Also, a relatively small number of surgeons participated in the ABM, which may limit the generalizability of the findings. The recommendations should be interpreted with caution and individualized according to the specific patient and surgical characteristics.

While there have been some studies comparing different THAs in neuro-spine surgeries, there is still a need for further research to provide a more comprehensive understanding of the effectiveness and safety of each agent in different bleeding situations and surgical procedures. The development of algorithms for THA usage in neuro-spine surgeries is a step towards standardization. However, there is a need for more guidelines and protocols to be developed based on high-quality evidence and implemented in hospitals to ensure consistency in THA usage and improve patient outcomes.

4.1. Clinical practice implications for neuro-spine surgeons

- Enhance preparedness for intraoperative bleeding by considering known risk factors, such as patient profile and procedure.
- Facilitate knowledge sharing in the operating room, including anesthetists and nurses, to ensure optimal support to the surgeon during surgery.
- Prioritize the direct contact of the hemostat with the bleeding site as the initial step in bleeding control.
- Ensure the appropriate selection and utilization of hemostatic products at the right time and in the correct manner.

5. Conclusion

Topical hemostatic agents are essential in neuro-spine surgery to control bleeding and minimize intraoperative and postoperative complications. The choice of THA depends on the bleeding site, situation, surgical procedure, and patient factors. As per the clinical experience of experts, ORC/Fibrillar emerged as the preferred choice of THA in neuro-spine surgery considering the cost implications. Based on available literature and expert opinion the two commonly used THAs in the neuro-spine segment are flowable gelatin + thrombin and ORC/Fibrillar. The algorithms developed here may be particularly useful in the Indian setting for selecting appropriate THAs in various bleeding sites and situations during neuro-spine procedures and are a crucial step towards ensuring cost-effectiveness and optimizing patient outcomes.

Funding/Support

This advisory board meeting was supported by J&J Ethicon Medical Devices. The opinions and recommendations expressed in this manuscript exclusively represent the perspectives of the authors. No financial contributions or affiliations from the J&J Ethicon division have contributed to shaping these viewpoints.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

We would like to thank Dr. Vernon Velho and Dr. Hrushikesh Kharosekar for their invaluable insights and contributions during the meeting and for review and approval of the manuscript. Dr. Dilip Paniker assisted in the content and review of the article independently and did not attend the Consensus meeting. Dr. Srirupa Das is an employee at JJ MedTech and MA Director, Independent reviewer of the article. The authors would like to thank Medulla Communications Pvt. Ltd. for providing medical writing assistance in the development of this manuscript.

References

[1] Haynes AB, Weiser TG, Berry WR, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. N Engl J Med 2009;360(5):491–9. https://doi.org/10.1056/NEJMsa0810119.
[2] Echave M, Oyagüez I, Casado MA. Use of Floseal®, a human gelatine-thrombin matrix sealant, in surgery: a systematic review. BMC Surg 2014;14(1):1–13. https://doi.org/10.1186/1471-2482-14-111.
[3] Rajagopalan V, Chouhan RS, Pandia MP, et al. Effect of intraoperative blood loss on perioperative complications and neurological outcome in adult patients undergoing elective brain tumor surgery. J Neurosci Rural Pract 2019;10(4): 631–40. https://doi.org/10.1055/s-0039-3399487.
[4] Cheriyan T, Maier 2nd SP, Bianco K, et al. Efficacy of tranexamic acid on surgical bleeding in spine surgery: a meta-analysis. Spine J 2015;15(4):752–61. https://doi.org/10.1016/j.spinee.2015.01.013.
[5] Nevelff DJ. Optimizing hemostatic practices: matching the appropriate hemostat to the clinical situation. AORN J 2012;96(5):S1–. https://doi.org/10.1016/j.aorn.2012.08.005.
[6] Stokes ME, Ye X, Shah M, et al. Impact of bleeding-related complications and/or blood product transfusions on hospital costs in inpatient surgical patients. BMC Health Serv Res 2011;11(1):1–13. https://doi.org/10.1186/1472-6963-11-135.
[7] Huang L, Liu GL, Kaye AD, et al. Advances in topical hemostatic agent therapies: a comprehensive update. Adv Ther 2020;37:4132–48. https://doi.org/10.1007/s12325-020-01467-y.
[8] Ferko N, Danker W, Gangoli G. A systematic approach to surgical hemostat use supports standardization and cost efficiencies. Healthcare Purchasing News 2017; 41(11):34–5.

[9] Massin P, Scemama C, Jeanrot C, et al. Does fibrin sealant use in total knee replacement reduce transfusion rates? a non-randomised comparative study. Orthop Traumatol Surg Res 2012;98(2):180–5. https://doi.org/10.1016/j.otsr.2011.10.012.
[10] Natour E, Suedkamp M, Dapunt OE, et al. Assessment of the effect on blood loss and transfusion requirements when adding a polyethylene glycol sealant to the anastomotic closure of aortic procedures: a case–control analysis of 102 patients undergoing Bentall procedures. J Cardiothorac Surg 2012;7(1):1–6. https://doi.org/10.1186/1749-8090-7-105.
[11] Testini M, Marzaioli R, Lissidini G, et al. The effectiveness of FloSeal® matrix hemostatic agent in thyroid surgery: a prospective, randomized, control study. Langenbecks Arch Surg 2009;394:837–42. https://doi.org/10.1007/s00423-009-0497-5.
[12] Le Huec JC, AlEissa S, Bowey AJ, et al. Hemostats in Spine Surgery: literature review and expert panel recommendations. Neurospine 2022;19(1):1–12. https://doi.org/10.14245/ns.2143196.598.
[13] American Society of Anesthesiologists Task Force on Perioperative Blood Management. Practice guidelines for perioperative blood management: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management. Anesthesiology. 2015; 122(2):241-75. 10.1097/ALN.0000000000000463.
[14] Lewis KM, Li Q, Jones DS, et al. Development and validation of an intraoperative bleeding severity scale for use in clinical studies of hemostatic agents. Surgery 2017;161(3):771–81. https://doi.org/10.1016/j.surg.2016.09.022.
[15] Sciubba DM, Khanna N, Pennington Z, et al. VIBe Scale: validation of the intraoperative bleeding severity scale by spine surgeons. Int J Spine Surg 2022;16(4):740–7. https://doi.org/10.14444/8304.
[16] Corral M, Ferko N, Hollmann S, et al. Health and economic outcomes associated with uncontrolled surgical bleeding: a retrospective analysis of the premier perspectives database. Clinicoecon Outcomes Res 2015;7:409–21. https://doi.org/10.2147/CEOR.S86369.
[17] Tsugawa AJ, Verstraete FJM. Suture materials and biomaterials. In: Verstraete FJM, Lommer MJ, editors. Oral and maxillofacial surgery in dogs and cats. Elsevier; 2012. p. 69–78.
[18] Mudge MC. Hemostasis, surgical bleeding, and transfusion. In: Auer JA, Stick JA, editors. Equine surgery. Elsevier; 2012. p. 35–47.
[19] Mısırlıoğlu S, Türkgeldi E, Yağmur H, Urman B, Ata B. Use of a gelatin-thrombin hemostatic matrix in obstetrics and gynecological surgery [published correction appears in Turk J Obstet Gynecol 2018 Dec;15(4):281]. Turk J Obstet Gynecol 2018;15(3):193–9. https://doi.org/10.4274/tjod.90217.
[20] Changela K, Papafragkakis H, Ofori E, et al. Hemostatic powder spray: a new method for managing gastrointestinal bleeding. Therap Adv Gastroenterol 2015;8(3):125–35. https://doi.org/10.1177/1756283X15572587.
[21] Spotnitz WD. Fibrin sealant: the only approved hemostat, sealant, and adhesive-a laboratory and clinical perspective. ISRN Surg 2014;2014:203943. https://doi.org/10.1155/2014/203943.
[22] King TJ, Sullivan EM. Surgery. In: Ballweg R, Sullivan EM, Brown D, Vetrosky D, editors. Physician Assistant. Elsevier; 2008. p. 411–73.
[23] Franceschini G. Use of oxidized regenerated cellulose as a hemostatic agent in neurosurgery: appraisals and recommendations to prevent postoperative complications and facilitate follow-Up. Surg Technol Int 2021;38:481–5. https://doi.org/10.52198/21.STI.38.NS1397.
[24] Lei H, Wen-hua R, Zhi-liang D, et al. Clinical hemostasis effect of a novel hemostatic material SURGICEL™ versus gelatin sponge in neurosurgery. Chin J Tissue Eng Res 2012;16(3):551–3.
[25] Gazzeri R, De Bonis C, Galarza M. Use of a thrombin-gelatin hemostatic matrix (Surgiflo) in spinal surgery. Surg Technol Int 2014;25:280–5.
[26] Gazzeri R, Galarza M, Neroni M, et al. Minimal craniotomy and matrix hemostatic sealant for the treatment of spontaneous supratentorial intracerebral hemorrhage. J Neurosurg 2009;110(5):939–42. https://doi.org/10.3171/2008.8.JNS17642.
[27] Eshghi P, Jenabzade A, Habibpanah B. A self-controlled comparative clinical trial to explore the effectiveness of three topical hemostatic agents for stopping severe epistaxis in pediatrics with inherited coagulopathies. Hematology 2014;19(6):361–4. https://doi.org/10.1179/1607845413Y.0000000135.
[28] Prabhu S, Prabhu S. Bespoke GelFoam Wafers: a practical and inexpensive alternative to oxycel for hemostasis during neurosurgery. Asian J Neurosurg 2019;14(2):483–6. https://doi.org/10.4103/ajns.AJNS_275_18.
[29] Menovsky T, Plazier M, Rasschaert R, et al. Massive swelling of Surgicel® Fibrillar™ hemostat after spinal surgery. Case report and a review of the literature. Minim Invasive Neurosurg 2011;54(5–6):257–9. https://doi.org/10.1055/s-0031-1284394.
[30] Claude Petit-Me J, Stawicki S P, Firstenberg M S, Marlin E. Biosurgical materials in neurosurgical applications: from pioneers to leaders. Contemporary applications of biologic hemostatic agents across surgical specialties. IntechOpen 2021. https://doi.org/10.5772/intechopen.95898.