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Traditional Thrombus Composition and Related Endovascular Outcomes: Catching up with the Recent Evidence

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Endovascular thrombectomy is the primary treatment for acute intracranial vessel occlusion and significantly improves recanalization success rate. However, achieving optimal recanalization remains a challenge. The histopathological components of thrombus composition play a crucial role in determining endovascular outcomes. This review aimed to consolidate the recent evidence on the impact of thrombus composition on mechanical properties and endovascular outcomes. The relationship between thrombus composition and mechanical properties was significant, with fibrin and/or platelet-rich thrombi being stiff, tough, elastic, and less deformable; fibrin-rich thrombi were sticky and had higher friction with the vessel wall. Erythrocyte composition was positively associated with successful recanalization, whereas lower platelet composition was associated with specific outcomes, such as the first-pass effect and complete recanalization. The number of thrombectomy device passes was possibly related to erythrocyte, platelet, and fibrin composition, with a smaller number of passes associated with erythrocyte-rich thrombi. Procedural time was consistently related to thrombus composition, with shorter times observed for erythrocyte-rich thrombi. The relationship between thrombus composition and secondary embolism remains inconclusive. Understanding the role of thrombus composition in endovascular outcomes is crucial to optimize stroke treatment. Although evidence suggests a link between thrombus composition and mechanical properties, further research is needed to establish stronger correlations and to reduce study variations. Exploring non-traditional thrombus components such as leukocytes and neutrophil extracellular traps is vital. Thrombus imaging could provide a practical solution for predicting thrombus composition before endovascular procedures. This review highlights the importance of thrombus composition for enhancing endovascular stroke treatment strategies.

Key Words: Thrombus; Histology; Thrombectomy; Stroke; Outcome

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INTRODUCTION

Endovascular thrombectomy is currently the treatment of choice for acute intracranial vessel occlusions. Although this procedure has led to significant improvements in recanalization success rates, some patients still do not achieve an acceptable level of recanalization. The mechanism of endovascular thrombectomy involves the "mechanical interaction" between the thrombectomy device and thrombus.[1-5] In this regard, the mechanical properties of the thrombus might be crucial in determining the success of endovascular treatment. Recognizing the mechanical properties of a thrombus can be critical for achiev-

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ing the best endovascular outcomes. One of the factors that contribute most to the mechanical properties of thrombi is their histopathologic composition.[6,7] Furthermore, advancements in thrombectomy devices have allowed the collection of retrieved thrombus samples, which can be analyzed for research purposes. A better understanding of thrombus composition may help overcome the current limitations of endovascular thrombectomy and may provide new insights into the optimal endovascular strategy.

The study of thrombus composition is a complex task because of the presence of various heterogeneities in related research. First, one reason for this is that thrombi contain a range of components, including erythrocytes, platelets, and fibrin, which have traditionally been regarded as the main components of thrombi.[8] However, recent research has highlighted additional components beyond traditional ones, such as leukocytes, neutrophil extracellular traps, von Willebrand factor, tissue factor, and a few coagulation factors.[9-14] The mechanical properties of thrombi can be affected by individual components or by interactions between them, leading to unexpected heterogeneity in thrombus characteristics based on histological composition. Second, although researchers have made progress in identifying and staining thrombus components, there is still no standardized approach to this task.[6] In the early days of research, classical staining methods such as hematoxylin and eosin staining and Martius Scarlet Blue staining were commonly used. However, recent studies have focused on immunohistochemical staining to identify specific thrombus components. The choice of staining method can vary depending on laboratory conditions. Third, there is currently no universally accepted method for quantifying thrombus composition. Thrombi can be described quantitatively as a fraction, which represents the ratio of a specific component to the total thrombus area, or qualitatively, in terms of dominance.[6] For instance, thrombi can be characterized as erythrocyte-rich, platelet-rich, or fibrin-rich based on the dominant component. However, there is no standard criterion for determining the dominance of specific components, and this approach may overlook the role of other components.

The goal of this review was to summarize key articles related to thrombus research, with a focus on the endovascular treatment of acute stroke. To achieve this, all relevant studies were gathered. While some studies covered multiple endovascular outcomes, this review organized the results according to specific outcomes for a better understanding. In addition, this review only covers 3 traditional thrombus components: erythrocytes, fibrin, and platelets, as they are the most significant factors affecting endovascular outcomes.[15] First, this article reviews the relationship between the composition of the thrombus and its mechanical properties. Subsequently, endovascular outcomes based on thrombus composition are discussed.

PART I. THROMBUS COMPOSITION AND ITS MECHANICAL PROPERTY

Several *in vitro* and *ex vivo* studies have demonstrated a relationship between thrombus composition and mechanical properties. Although various physical concepts can be used to understand the mechanical properties of thrombi, such as stiffness, hardness, deformability, viscosity, elasticity, toughness, fragility, and stickiness, stiffness is the most commonly represented mechanical property of thrombus. The stiffness of a thrombus can be analyzed in 2 different ways: compression and tension (stretching). Tensional characteristics are related to viscoelasticity and fragility, which contribute to thrombus fractures. This section reviews the key experimental studies on thrombus composition to determine its mechanical properties.

Stiffness

Compression

Boodt et al.[16] (2021) conducted an unconfined compression test on 41 thrombi obtained through the thrombectomy procedure. They discovered that the tangent modulus at 75% strain (E_{t75}), a marker of thrombus stiffness, was significantly correlated with the presence of fibrin and/or platelets (fibrin/platelets), erythrocytes, and platelets. The study revealed that the fibrin/platelet composition in thrombi was associated with increased stiffness, whereas erythrocytes had the opposite effect. Johnson et al.[17] (2020) prepared 2 types of thrombus analogs: platelet-contracted clots (PCCs) and non-contracted clots (NCCs). PCCs were prepared by combining blood mixtures of various hematocrit values with platelet-rich plasma, while NCCs were prepared under the same conditions but with platelet-poor plasma. The mechanical properties of thrombi are influenced by platelet-driven contractions, which tighten the fibrin network, expel serum from the thrombus, and reduce its volume. In

their experiment, PCCs exhibited an earlier onset point on the stress-strain curve, indicating that they were deformed earlier under the applied force and resisted further deformation sooner. Overall, PCCs were found to be stiffer than NCCs, possibly because of platelet-driven contraction. Cruts et al.[18] (2023) also discovered similar stress-strain relationships for thrombus analogs. Compressive stiffness was higher in fibrin-rich thrombi (0% erythrocyte composition) than in erythrocyte-rich thrombi (>90% erythrocyte composition).

Weafer et al.[19] (2019) investigated the extent to which stent struts could indent thrombi, which is a measure of the compressive stiffness of clots. To conduct their research, the authors prepared various thrombus analogs with hematocrit levels ranging from 0% to 80%. They used a steel indenter tip to indent the thrombi, and the indentation depth increased as the hematocrit level increased. The results showed that the stiffness of thrombi decreased significantly as erythrocyte content increased. In contrast, strut indentation during the embedding period decreased as erythrocyte content increased. This suggests that the benefit of embedding time is more pronounced for erythrocyte-poor thrombi. Thrombus imaging analysis showed a trend of increasing integrated thrombus volume with increasing erythrocyte content. Machi et al.[20] (2017) also reported that larger white thrombi were not penetrated by the stent struts and remained on the side of the stent compressed against the vessel wall.

Tension, viscoelasticity, and fracture toughness

The rupture and fracture of thrombi can reveal their tensional characteristics and viscoelasticities. Tutwiler et al.[21] (2020) investigated the mechanism and toughness of thrombus rupture with human blood plasma-derived fibrin thrombi, quantifying toughness through the critical energy release rate during cracked fibrin gel rupture. Liu et al.[22] (2021) calculated the fracture energy for whole blood thrombi and platelet-poor thrombi. The fracture energy was lower for platelet-poor thrombi, indicating that the fracture toughness was lower in erythrocyte-rich thrombi. Fereidoonnezhad et al.[23] (2021) conducted experiments to investigate the relationship between thrombus composition and fracture toughness, specifically focusing on composition-dependent fracture behavior. They prepared 3 different types of thrombi with varying fibrin content: high fibrin (5% of hematocrit), medium fibrin (20%), and low fibrin (40%). The results showed that fracture toughness significantly increased with higher fibrin content, indicating that thrombi with a higher erythrocyte content were more susceptible to tearing than those with a higher fibrin content.

Cahalane et al.[7] (2023) investigated the tensile properties of thrombi using a tensile mold. They prepared thrombus analogs with different erythrocyte compositions (5%, 10%, 20%, 40%, 60%, and 80%) from human blood. The tensile stiffness was quantitatively measured and showed a decrease with increasing erythrocyte composition in the thrombi. Gersh et al.[24] (2009) previously demonstrated that the erythrocyte composition of thrombi affects the formation of thicker fibrin fibers, which consequently impacts the viscoelastic properties. With thrombus analogs of varying erythrocyte levels, a higher erythrocyte composition increased the viscous component of thrombi relative to the elastic component, indicating a less elastic thrombus.

Thrombus fragmentation exhibits tensile characteristics associated with reduced elasticity and low fracture toughness, which are also observed in erythrocyte-rich thrombi. In a study conducted by Freiherr von Seckendorff et al.[25] (2022), *in vitro* thrombectomy was performed on erythrocyte-rich and platelet-rich thrombi using a commercially prepared flow model equipped with a distal thrombus filter. The results revealed a significantly higher number of embolic fragments deposited on the output filter membrane after thrombectomy for erythrocyte-rich thrombi.

Friction

Friction between the thrombus and vessel wall can have a significant impact on the success of thrombectomy. Thrombus with high friction or a strong adhesion to the vessel wall may act as a sticky thrombus, making it more challenging to retrieve it.[9] Gunning et al.[26] (2018) studied the friction of thrombi using an angle-changeable stainless-steel plate and calculated the coefficient of friction to determine the friction characteristics of thrombi with varying erythrocyte compositions (0%, 5%, 20%, 40%, and 80%). Their findings revealed that fibrin-rich thrombi (composition <20% erythrocytes) had a significantly higher coefficient of friction than those with a composition of ≥20% erythrocytes. This suggests that fibrin-rich thrombi are more frictional than erythrocyte-rich. The reproducibility of these results was demonstrated through experiments on bovine aortic surfaces.

Summary

The relationship between thrombus composition and mechanical properties was significant. In the majority of exper-

iments, fibrin or platelets are typically employed as a counterpart to erythrocytes. However, fibrin/platelet-rich thrombi, which were erythrocyte-poor, were stiff, tough, elastic, and less deformable. Additionally, the stent strut did not penetrate deeply into or integrate well with the fibrin/platelet-rich thrombi. Fibrin-rich thrombi were sticky and had higher friction with the vessel wall. These mechanical properties are believed to be the reason why fibrin/platelet-rich thrombi are difficult to retrieve during thrombectomy.

PART II. THROMBUS COMPOSITION AND ENDOVASCULAR OUTCOME

Endovascular Outcomes in Animal and *In Vitro* Models

Yuki et al.[27] (2012) conducted thrombectomy procedures on a swine animal model using an outdated device (Merci retriever) to remove two types of thrombi: erythrocyte-rich and fibrin-rich thrombi. The composition of thrombi was not quantitatively analyzed; rather, their histology was examined grossly. The results showed that the number of attempts with the device was significantly higher for the fibrin-rich thrombi. Furthermore, successful recanalization based on Thrombolysis In Myocardial Infarction grades II and III was much lower for fibrin-rich thrombi, and it took significantly longer to achieve. An *in vitro* experiment demonstrated a similar association between thrombus composition and endovascular outcomes. Additionally, Freiherr von Seckendorff et al.[25] (2022) used a flow model to show that a higher number of stent retriever passes and longer procedural times were necessary for platelet-rich thrombi.

Recanalization

The impact of thrombus composition on recanalization outcomes can be assessed using 2 methods. The first involves comparing the composition of thrombi based on the recanalization results. Typically, the mean or median values of specific thrombus components were examined between dichotomized recanalization end points. For example, Hashimoto et al.[28] (2016) compared the mean erythrocyte composition between patients who achieved successful recanalization (modified Thrombolysis In Cerebral Infarction [mTICI] grade 2b or 3) and those who did not. The results showed that erythrocyte composition was significantly higher in the successful recanalization group (57% *vs.* 47%; P=0.042). Additionally, erythrocyte composition was independently associated with successful recanalization (adjusted odds ratio [aOR], 4.35; 95% confidence interval [CI], 1.19–19.36; P=0.026). A cutoff value for erythrocyte composition of >64% was identified as predictive of successful recanalization. In contrast, fibrin/platelet composition did not differ significantly based on successful recanalization (42% *vs.* 48%; P=0.166). Shin et al.[29] (2018) investigated thrombus composition based on the Arterial Occlusive Lesion (AOL) score. The study revealed that erythrocyte composition had a higher mean value (37% *vs.* 20%; P=0.001) in patients with better recanalization (AOL score 2–3).

Delvoye et al.[30] (2022) concentrated on the platelet composition within the thrombus. Using an immunoassay to measure glycoprotein VI levels, they quantitatively determined the platelets in the thrombus. Notably, the researchers compared the platelet composition between patients who experienced the first-pass effect (mTICI grade 2c or 3 achieved by a single pass of the device) and those who did not. The study found that the number of platelets was significantly lower in cases with the first-pass effect (0.098 *vs.* 0.111 ng/mg; P<0.001), suggesting that platelet-poor thrombi are associated with the likelihood of the first-pass effect. Additionally, a higher platelet count was significantly associated with lower mTICI grades (aOR, 0.69; 95% CI, 0.53–0.89). In contrast, Sporns et al.[31] (2017) discovered that the primary component of the thrombus did not have an effect on the success of recanalization. The composition of erythrocytes (31.0% *vs.* 13.5%; P=0.096) and fibrin (57.0% *vs.* 71.5%; P=0.128) were similar between patients who successfully underwent recanalization and those who did not.

In a meta-analysis of 6 related studies, a higher erythrocyte composition was associated with a better angiographic outcome, with a mean difference of erythrocyte composition 9.6% (95% CI, 3.9–15.3; P=0.008).[32]

The second approach involves comparing recanalization results based on the thrombus type. To achieve this, thrombi are typically classified according to their dominant composition. However, because there is no universally recognized method for determining dominance, this classification may be somewhat arbitrary. Shimizu et al.[33] (2022) divided thrombi into platelet-rich/poor and erythrocyte-rich/poor categories based on platelet and erythrocyte composition, respectively. The presence of platelets in the thrombus was confirmed by immunohistochemistry, with thrombi containing more than 24.3% platelets designated as platelet-rich. Complete recanalization (mTICI grade 3) was lower in

platelet-rich thrombi than in platelet-poor thrombi (32.4% *vs.* 59.5%; P=0.035). However, there was no significant difference in complete recanalization based on erythrocyte composition, with rates of 48.6% for erythrocyte-rich and 43.2% for erythrocyte-poor thrombi (P=0.816), as determined by a cut-off value of 34.7%. Maekawa et al.[34] (2018) divided thrombi into erythrocyte-rich and fibrin-rich categories, but did not provide a specific criterion for this classification. Successful recanalization (mTICI grade 2b or 3) was comparable between the 2 types of thrombi, with 100% for erythrocyte-rich thrombi and 96% for fibrin-rich thrombi (P=0.999).

A unique per-pass analysis can provide additional insights into the impact of thrombus composition on the outcomes of thrombectomy treatment. In a study conducted by Duffy et al.[35] (2019), thrombus fragments were examined after each thrombectomy device pass. Notably, a higher concentration of erythrocytes was observed in thrombi retrieved during passes 1 and 2 than in those retrieved during passes 3 to 6 (P=0.001). Conversely, fibrin composition exhibited an inverse relationship (P=0.001). The interpretation of these findings suggests that thrombi with a higher erythrocyte content are more easily retrieved and removed earlier during the procedure.[6,8,36,37]

Number of Thrombectomy Device Passes

Maekawa et al.[34] (2018) discovered that there was a higher number of thrombectomy device passes in fibrin-rich thrombi compared to erythrocyte-rich thrombi (2.9 *vs.* 1.8; P=0.020). Shimizu et al.[33] (2022) found that the number of device passes was greater in platelet-rich thrombi than in platelet-poor thrombi (1.5 *vs.* 1.0; P=0.019). However, there was no significant difference in the number of device passes between erythrocyte-rich and erythrocyte-poor thrombi (1.0 *vs.* 1.0; P=0.375). Delvoye et al.[30] (2022) also demonstrated a link between platelet composition and the number of device passes (OR, 1.11; 95% CI, 1.01–1.23); however, this association was not significant in the multivariable analysis (aOR, 1.09; 95% CI, 0.99–1.21).

Kitano et al.[10] (2022) conducted a study to compare the endovascular outcomes between fresh (<1 day) and older (1–5 days) thrombi. The results showed that patients with older thrombi required more device passes (2.0 *vs.* 1.0; P<0.001). Additionally, the study found that first-pass recanalization (achieving mTICI 2b or 3 with a single device pass) was less likely in older thrombi (45% *vs.* 72%; P=0.003). Researchers suggest that the higher number of device passes in older thrombi may be due to their higher platelet count and lower erythrocyte composition, although this is an indirect finding. Furthermore, a previous study by Duffy et al.[35] (2019) found that thrombus fragments from passes 1 and 2 had higher erythrocyte and lower fibrin compositions, which may explain the lower number of device passes required for erythrocyte-rich (or fibrin-poor) thrombi.

Time to Successful Recanalization and Procedural Time

The research conducted by Simons et al.[38] (2015) investigated the connection between the time from stroke onset to successful recanalization (onset-to-recanalization time) and procedural time based on erythrocyte and fibrin dominance in thrombi. The thrombus was categorized as erythrocyte-dominant (erythrocyte>fibrin), equally dominant (erythrocyte=fibrin), or fibrin-dominant (erythrocyte<fibrin). The procedural time was significantly longer for equally dominant thrombi (70.3 minutes), and no relationship was observed between any type of thrombus and onset-to-recanalization or procedural time.

According to Sporns et al.[31] (2017), there was a significant correlation between fibrin composition of the thrombus and procedural time (r=0.484; P<0.001), while erythrocyte composition of the thrombus was inversely correlated with procedural time (r=0.491, P<0.001). Maekawa et al.[34] (2018) analyzed time profiles according to thrombus composition and found that procedural (24.5 *vs.* 44.0 minutes; P<0.010) and door-to-recanalization (86.5 *vs.* 110.0 minutes; P=0.040) times were significantly shorter in patients with erythrocyte-rich thrombi. Shimizu et al.[33] (2022) also observed that puncture-to-recanalization time was significantly shorter for erythrocyte-rich thrombi (45.0 *vs.* 75.0 minutes; P=0.007). However, in that study, the puncture-to-recanalization time was not significantly longer for platelet-rich thrombi (71.0 *vs.* 53.0 minutes; P=0.160). Delvoye et al.[30] (2022) showed that a higher platelet composition is associated with a longer procedural time. In a meta-analysis of 5 related studies, higher erythrocyte composition was associated with shorter procedural time with a mean difference of procedural time 13.2 minutes (95% CI, 1.3–25.1; P=0.037).[32]

Secondary Embolism

Thrombus fragmentation is a key observation derived from its mechanical properties and is the most direct indicator of thrombus fragility. This phenomenon can have negative

effects on endovascular outcomes by causing downstream occlusion through secondary embolisms. This is a common occurrence during thrombectomy. In the research field, secondary embolism is defined as any occlusion that occurs distal to the original occlusion site after thrombectomy attempts.[39]

The relationship between thrombus composition and secondary embolism remains debatable. For 54 patients, Ye et al.[40] (2020) found that patients with secondary embolism had a higher erythrocyte composition (42.9% *vs*. 26.8%; P=0.045), but this was not statistically significant when comparing dichotomized values (erythrocyte-rich or not; 63.2% *vs*. 42.9%; P=0.154) or in multivariable analysis (aOR, 35.4; 95% CI, 0.73–1,718.99; P=0.072). Other thrombus compositions, such as fibrin (33.6% *vs*. 40.2%; P=0.273) and platelets (16.2% *vs*. 22.4%; P=0.130), were not significantly different between patients with and without secondary embolism. In contrast, from a study of 180 patients, Sporns et al.[31] (2017) reported that secondary embolism was associated with lower erythrocyte (10.0% *vs*. 35.0%; P<0.001) and higher fibrin (80.0% *vs*. 55.0%; P<0.001) levels. This finding appears to contradict the results of *in vitro* studies, which showed that erythrocyte-rich thrombi are less stiff and more deformable, potentially resulting in less fragmentation.

Thrombus migration is a noteworthy clinical observation that likely indicates fragility or other mechanical properties of the thrombus. This suggests that if thrombus migration is caused by spontaneous fragmentation, the thrombus may have a histological background similar to that of fragile thrombi. Thrombus migration can be directly detected by comparing pre-procedural images with procedural angiography. If the thrombus's location on the preprocedural computed tomography angiography has moved to a more distal position on the first procedural angiography, it can be

Table 1. Summary of key results from studies of the association between thrombus composition and endovascular outcomes

Composition	References	Study model	Recanalization ↑	Pass number ↓	Procedural time ↓	Secondary embolism ↑
Qualitative	Yuki 2012[27]	Experimental; animal	Erythrocyte-rich	Erythrocyte-rich	Erythrocyte-rich	
	Freiherr von Seckendorff 2022[25]	Experimental; *in vitro*		Erythrocyte-rich	Erythrocyte-rich	Erythrocyte-rich
	Simons 2015[38]	Clinical			No association	
	Hashimoto 2016[28]	Clinical	Erythrocyte-rich			
	Maegerlein 2018[41]	Clinical				Erythrocyte-rich
	Maekawa 2018[34]	Clinical	No association	Erythrocyte-rich	Erythrocyte-rich	
	Ye 2020[40]	Clinical				No association
	Shimizu 2022[33]	Clinical	Platelet-poor	Platelet-poor	Erythrocyte-rich	
Quantitative	Hashimoto 2016[28]	Clinical	Higher erythrocyte			
	Sporns 2017[31]	Clinical	No association		Higher erythrocyte; lower fibrin	Lower erythrocyte; higher fibrin
	Maegerlein 2018[41]	Clinical				Higher erythrocyte
	Shin 2018[29]	Clinical	Higher erythrocyte			
	Duffy 2019[35]	Clinical	Higher erythrocyte; lower fibrin			
	Sporns 2019 (also 2021)[42,43]	Clinical				Higher erythrocyte; lower fibrin
	Ye 2020[40]	Clinical				Higher erythrocyte
	Delvoye 2022[30]	Clinical	Lower platelet	Lower platelet	Lower platelet	
	Kitano 2022[10]	Clinical	Fresh	Fresh		

Supplementary Table 1 presents comprehensive information that has been derived from the manuscript, providing a clear explanation of the research findings. Furthermore, in the Supplementary Table 1, you will find a comprehensive list of histological components, along with the analysis methods used (both qualitative and quantitative variables), and the staining methods employed in the studies.

considered a migrated thrombus.[41]

A study conducted by Maegerlein et al.[41] (2018) revealed that the composition of erythrocytes and fibrin/platelets did not differ between patients with and without thrombus migration in the middle cerebral artery occlusion (41% *vs*. 37% for erythrocytes, P=0.230; 54% *vs*. 57% for fibrin/platelets, P=0.240). However, upon further analysis, the researchers found that erythrocyte-rich thrombi (>60% erythrocyte composition) were more prevalent in the thrombus migration group (36.4% *vs*. 5.7%, P=0.003). This finding was consistent with the results reported by Sporns et al.[42,43] (2019 and 2021), who also observed higher erythrocyte composition (50.0% *vs*. 26.0%, P<0.001) and lower fibrin composition (43.5% *vs*. 62.0%, P<0.001) in thrombi with migration. Moreover, higher erythrocyte composition was found to be an independent factor for thrombus migration (aOR, 1.03; 95% CI, 1.02–1.05; P<0.001).

Summary

The relationship between erythrocyte composition and successful recanalization was positive, while lower platelet composition was associated with specific outcomes, such as the first-pass effect and complete recanalization (Table 1, Supplementary Table 1). Furthermore, the number of thrombectomy device passes was possibly related to erythrocyte, platelet, and partly fibrin composition. Although limited, a smaller number of passes was associated with erythrocyte-rich (or platelet- and fibrin-poor) thrombi. Procedural time was consistently related to thrombus composition, with shorter times observed for erythrocyte-rich thrombi. However, it remains inconclusive whether thrombus composition is associated with secondary embolism, whereas thrombus migration is consistently associated with higher erythrocyte composition.

CONCLUSIONS AND FUTURE DIRECTIONS

Based on the available evidence, it is clear that the study of thrombus composition is a crucial aspect of endovascular treatment for acute stroke. Although there are limitations and differences in the studies, thrombus composition has been shown to have a partial and significant connection with mechanical properties and endovascular outcomes after thrombectomy procedures. However, more research is needed to establish a stronger connection and reduce variations between studies. Furthermore, it is essential to explore beyond the conventional components of thrombi, such as erythrocytes, platelets, and fibrin, to understand endovascular responses during thrombectomy procedures. Recently, the concept of immunothrombosis, mediated by leukocytes or neutrophil extracellular traps, has gained significance. Although this topic is not explicitly covered in this paper, it merits a comprehensive review in the near future.

Histological analysis of a thrombus is not feasible until after endovascular procedures and can be extremely time-consuming, restricting its applicability in establishing an endovascular strategy. Thrombus imaging can serve as a viable solution to this problem. By preprocedural imaging of the thrombus, it is possible to predict its composition, thereby enabling the prediction of endovascular responses through thrombectomy. Understanding the composition of thrombi and relevant study methodologies can provide a fundamental basis for research in thrombus imaging.

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Ethics Statement

This study was exempted from the review by the institutional ethics committee. This article does not include any information that may identify the person.

Conflicts of Interest

JHB has been the assistant editor of *Neurointervention* since 2018. However, he/she has not been involved in the peer reviewer selection, evaluation, or decision process of this article. No potential conflict of interest relevant to this article was reported. No other authors have any conflicts of interest to disclose.

Author Contributions

Concept and design: JHB. Analysis and interpretation: JHB. Data collection: JHB. Writing the article: JHB. Critical revision of the article: JHB. Final approval of the article: JHB. Obtained funding: JHB. Overall responsibility: JHB.

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