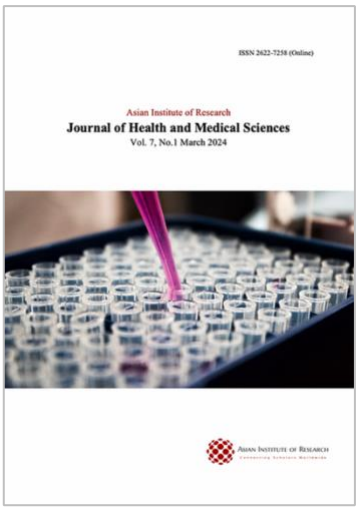

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Transcranial Doppler Findings in Myeloproliferative Diseases (Polycythemia Vera and Essential Thrombocytosis): A Systematic Review

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Abstract
Background and aims: Myeloproliferative neoplasms (MPN) are rare hematologic diseases that require early diagnosis to prevent thrombotic events. Only a few studies have investigated transcranial Doppler (TCD) ultrasonography among these population groups. Following the PRISMA Guidelines, we reviewed the utility of TCD in Polycythemia vera (PV) and Essential Thrombocytosis (ET) patients in the context of cerebral blood flow and detection of microembolic signals (MES). Methods: This systematic review focuses on the application of TCD in MPN. By incorporating findings from one observational study, one prospective study, and three case reports, the review establishes that while TCD is not a primary tool for diagnosing PV and ET, it plays a crucial role in monitoring cerebrovascular complications, assessing thrombotic risk, evaluating treatment responses, and facilitating research related to these conditions. Results: This review incorporates findings from a total of 63 patients. 3.2% had ischemic stroke and 1.6% had transient ischemic attack with a total of 4.8% stroke risk. High-intensity transient signals (HITS) were common in 22% of patients wherein they had elevated hemoglobin, hematocrit, and platelet values. Following treatment and normalization of blood panels, 31.7% had improved cerebral perfusion with normal flow velocities. 3.2% had elevated flow velocities linked to blood flow obstruction. There was significant clinical improvement among the study population, with 17.5% becoming asymptomatic with the disappearance of MES. Conclusions: The judicious use of TCD can enhance a comprehensive diagnostic and monitoring strategy, complementing traditional clinical and laboratory assessments in the management of MPN specifically PV and ET.

Keywords: Transcranial Doppler, Cerebral Hemodynamics, Microembolic Signals, Polycythemia Vera, Essential Thrombocytosis

1. Introduction

Myeloproliferative neoplasms (MPN) are a group of hematologic disorders arising from the aberrant proliferation of one or more terminal myeloid cell lineages in the peripheral circulation. The three classic *BCR-ABL1* negative MPNs include essential thrombocythemia (ET), polycythemia vera (PV), and primary myelofibrosis (PMF) (Arber et al, 2016). These diseases are also characterized by JAK2 mutation, leading to sustained activation of the JAK2

kinase, subsequently causing excess blood cell production independent of erythropoietin (Lu et al, 2023). This mutation is correlated with increased risk of cerebrovascular complications, predominantly due to the hypercoagulability state that is observed in these individuals.

The prevalence of MPNs is uncertain due to limited incidence estimates and a lack of consistent, repeatable data. Both PV and ET are diagnosed at a median age of sixty years. PV predominantly affects males than females (male to female ratio: 1.8: 1) with an annual incidence estimates that range between 0.4% and 2.8% per 100,000 individuals. Meanwhile, ET has higher prevalence among females, with a male-to-female ratio of 1:2, and an annual incidence estimate ranging between 1.2 and 2.5 per 100,000 individuals (Srour et al, 2017). Due to the lower prevalence of PMF, this current review would only include ET and PV patients.

A meta-analysis of 13,436 newly diagnosed patients with MPN revealed that thrombosis (20%) and hemorrhage (16.2%) are frequent initial manifestations of the disease. The disease is associated with a higher risk for arterial or venous thrombosis than the general population. Additionally, the study revealed that the combined prevalence of arterial and venous thrombosis in PV was 28.6%, while that of bleeding was 6.9%. In contrast, the pooled prevalence in ET was 20.7% and 7.3% for arterial and venous thrombosis and hemorrhage, respectively (Rungjirajittranon et al, 2019).

While complications abound in the context of PV and ET, particularly involving ischemic cerebrovascular events, a complete understanding of the mechanisms behind these complications remains elusive (Spivak, 2002; Elliott & Tefferi, 2005; Barbui et al., 2013; Falanga & Marchetti, 2014). Consequently, transcranial Doppler (TCD) has become a valuable instrument for observing cerebral blood flow and identifying initial indications of cerebrovascular dysfunction. TCD is a relatively inexpensive, non-invasive, repeatable procedure that provides rapid and real-time measures of cerebrovascular function (Purkayastha & Sorond, 2012). TCD is used to assess cerebral hemodynamics, including cerebral blood flow velocity and pulsatility indices. It is also used to investigate cerebrovascular autoregulation and the presence of microembolic signals (MES) or high-intensity transient signals (HITS).

Exploring the cerebrovascular impact of PV and ET and their connection with TCD findings has important treatment implications. Yet, limited articles delve into the relationship between TCD findings and these conditions. This systematic review seeks to investigate this link and aims to uncover connections between specific blood parameters and TCD results, aiming to provide insights into the mechanisms contributing to cerebrovascular complications in patients with PV and ET. Understanding these correlations can enhance our comprehension of how changes in blood composition relate to cerebrovascular events. The study also aims to evaluate the ability of TCD to predict the occurrence of cerebrovascular events in patients with PV and ET. By determining whether TCD findings can serve as predictive markers, the study aims to contribute valuable information for clinicians in identifying individuals at an elevated risk of cerebrovascular complications. This insight could impact the management and preventive strategies for these patients.

2. Methodology

2.1. Search strategy

Searches were conducted in the following scientific databases: PubMed, the Cochrane Library, and Google Scholar. The keywords used were "polycythemia vera," "essential thrombocytosis," and "transcranial Doppler" to search titles and abstracts. Duplicate terms included "TCD" and "polycythemia rubra vera."

During the search on these databases, the following filters were applied: type of study (observational studies, prospective studies, cohort studies, clinical studies, and case reports), language (English), and study subjects (individuals >18 years of age). The reference lists of the included papers were also manually reviewed for any additional eligible studies.

However, despite the thorough and intensive search, minimal studies were shown to meet the inclusion and exclusion criteria. PV and ET are relatively rare conditions, and specific clinical scenarios or complications associated with these diseases may not be well documented in large-scale clinical studies or trials involving TCD. Case reports can highlight these rare or unusual occurrences, offering a deeper understanding of the diverse clinical presentations and outcomes associated with PV and ET. Case reports often emphasize clinical relevance and real-world applicability; they showcase specific patient experiences and outcomes, which may benefit clinicians seeking guidance on properly managing similar situations.

In the context of PV and ET, which both have multifaceted complications, case reports can illustrate less common cerebrovascular complications, which may have yet to be extensively studied. They can expound on knowledge about these complications, helping clinicians and researchers recognize them in practice.
While case reports can contribute valuable information to a systematic review, it is essential to acknowledge their limitations. They are anecdotal and may lack the scientific rigor of controlled studies. Therefore, their inclusion in this study was balanced with critically evaluating their quality and relevance to the research question. Including case reports in this study was done judiciously.

2.2. Eligibility criteria and clinical case definitions

Included studies were those that described cerebral hemodynamics using TCD among patients diagnosed with PV and ET done among patients aged 18 years and older of both sexes and any ethnicity. They were published from database inception up to April 30, 2022. Study outcomes included TCD parameters (including mean flow velocity and MES monitoring) and hematocrit, hemoglobin, and platelet values.

Studies with other hematologic conditions or severe cardiovascular disease were excluded Studies with pregnant patients and those with severe coexisting medical conditions were also excluded. Studies not in English, animal studies, unfinished and unpublished trials, and those not from primary literature such as review articles, editorials, commentaries, or meta-analyses were likewise excluded.

2.3. Selection process

Upon removing duplicates, studies resulting from the initial search were screened for eligibility through their titles and abstracts by the investigator. Studies that were not relevant to the objectives of this review were excluded. A second round of screening was performed based on the complete text, and the list of studies to be included in the systematic review was finalized after the fact. References identified during the second round of screening were again screened for a third time. For comprehensiveness, the reference lists of included studies and other previously published meta-analyses were cross-checked for additional studies that could meet the eligibility criteria.

2.4. Outcomes assessed

Data items that were extracted included the following: general information (author, year of publication, country) and study characteristics in terms of study design, population, sample size, age and sex of study participants, and a diagnosis of polycythemia vera or essential thrombocytosis. TCD parameters of interest included any of the following: cerebral mean flow velocities (MFV) in the middle cerebral artery (MCA), anterior cerebral artery (ACA), posterior cerebral artery (PCA), basal cerebral artery (BA), and MES or high-intensity transient signals (HITS).
Other study outcomes included changes in TCD parameters and hematocrit, hemoglobin, and platelet values.

2.5. Data analysis

A pre-specified electronic data collection sheet was used for all included studies to retrieve pertinent information. Descriptive statistics in frequency and percentages were used to analyze study outcomes and will be computed using Microsoft Excel.

3. Results

3.1. Characteristics of the retrieved studies

After a thorough selection process across five databases (Science Direct, Google Scholar, PubMed, Cochrane Library, and Journal Storage), six articles (three retrieved from PubMed and three from Google Scholar) matched all the characteristics outlined in the inclusion and exclusion criteria. Studies that did not meet the inclusion criteria based on age and diagnosis were excluded from the review. Moreover, animal studies, unfinished and unpublished trials, and those not from primary literature, such as review articles, editorials, commentaries, or meta-analyses, were also excluded after the removal of duplicates and exclusion of studies with meta-analyses. Five articles were screened based on their title and the contents of their respective abstracts. All five articles passed the eligibility criteria and were subsequently included in the study. Fig. 1 illustrates the search strategy for selecting studies for the review.

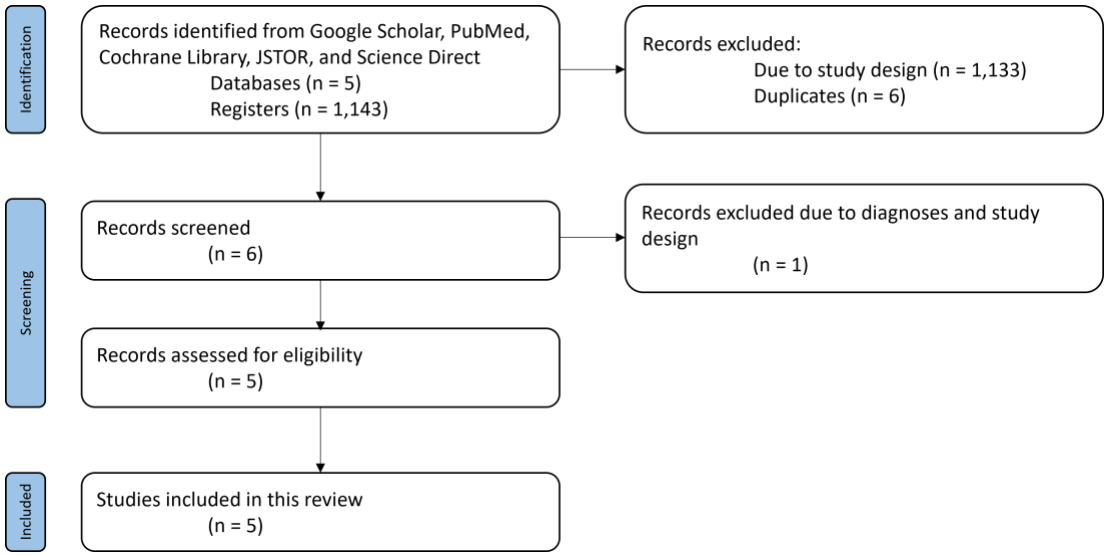

Figure 1: Search strategy for the selection of studies using PRISMA Method

Table 1 shows the summary of results from the articles collated, which includes details of the authors, year published, study design, Doppler machine used, and outcomes assessed in the respective papers.

Table 1: Summary of Studies

Author & Year Published	Study Population	Study Design	Doppler machine used	Outcomes Assessed
Fiermonte et al. (1993)	PV	Observational study *(N = 20)*	CW Doppler Velocimeter D800; TC 2-64b	• Mean flow velocities (MCA, ACA, PCA and BA)
Del Sette et al. (1995)	PV	Case report *(N = 1)*	TCD 64 EME	• Mean flow velocities (MCA) • MES in MCA
Segura et al. (2000)	PV	Case report *(N = 1)*	DWL-multidop X4	• Mean flow velocities (MCA) • MES in MCA
Blaser et al. (2001)	ET	Case report *(N = 1)*	*Not specified*	• MES in MCA
Cinar et al. (2020)	ET	Prospective study *(N = 40)*	Sonara TCD system Care Fusion, San Diego, CA, USA	• Mean flow velocities (MCA) • MES in MCA

Table 2 shows the pre- and post-therapy clinical features of the study population, the neuroimaging and treatment employed.

Table 2: Clinical features of PV and ET patients

Author and Year	Pre-therapy clinical features	Neuroimaging	Treatments employed	Post-therapy clinical features
Fiermonte et al. (1993)	Hypertension, headache, asthenia, itching, splenomegaly (2-5cm), scotomas, blushed face, cyanosis, vertigo, gouty arthritis, paresthesia, confusional state	*None*	• Phlebotomies • Pipobromanum 50-75mg • Dipyridamolum 150-225mg	Hypertension, periodic headache, splenomegaly (1cm), gouty arthritis
Del Sette et al. (1995)	Left-sided headache Right brachiorural paresis	Left hemispheric infarction with hemorrhagic transformation in the area of the lenticulostriate arteries and posterior branches of the right MCA	• Isovolemic hemodilution • Pentoxifylline 800mg • LMW Dextran 500ml • Heparin 24,000 IU • Busulfan 4mg • Ticlopidine 500mg	Mild right hemiparesis
Segura et al. (2000)	Left brachial paresis	Right hemispheric infarction of the posterior division of the MCA	• Ticlopidine • Acenocumarol INR	Asymptomatic
Blaser et al. (2001)	Recurrent right-sided paresthesia of the extremities and face, blurred vision on the right, dizziness, headache	Normal	• ASA 100mg/day • Hydroxycarbamide	Asymptomatic
Cinar et al. (2020)	*Not specified in the study*.	*None*	• Low dose aspirin • Hydroxyurea • Anagrelide	*Not specified in the study*.

Of the five studies reviewed, three were case reports wherein there were two cases of PV and one case of ET (Del Sette et al., 1995; Segura et al., 2000; Blaser et al., 2001), one was an observational study with a sample size of 20 newly diagnosed PV patients (Fiermonte et al., 1993), and another was a prospective case-control study with a sample size of 40 ET patients, age and sex-matched with 40 healthy controls (Cinar et al, 2021). In total, 63 patients were included in this review; 27 were male, and 36 were female. The median age of the participants is 58.89 years.

In utilizing transcranial Doppler, readings were performed using various Doppler models, including the following: CW Doppler Velocimeter D800 and TC 2-64b, TCD 64 EME, DWL-multidop X4, and Sonara TCD system Care Fusion. One study did not specify the TCD machine used (Blaser et al, 2001). There was no mention of the credentials of sonographers in any of the investigations.

Polycythemia vera was diagnosed according to the criteria of the Polycythemia Vera Study Group (PVSG) (Fiermonte et al., 1993), or confirmed through bone marrow examination (Segura et al., 2000) or through hematological screening (Del Sette et al., 1995).

Meanwhile, essential thrombocytosis was diagnosed according to the WHO 2008 diagnostic criteria for ET (Cinar et al, 2021). Platelet function tests, such as template bleeding time, platelet glass retention, quantitative clot retraction, and induced platelet aggregation by ADP, were also performed (Blaser et al, 2001).

The outcomes measured across three studies investigating patients with PV were in congruence with each other. The blood velocities in the MCA were measured in 62 patients from all the studies, except one (Blaser et al, 2001), which only investigated MES. 20 subjects from Fiermonte et al.'s study also measured the blood velocities in the ACA, PCA, and BA.

All five studies described the TCD findings and blood parameters outlined in Table 3. Elevated hematocrit and hemoglobin values in all 22 PV cases (Del Sette et al., 1995; Segura et al., 2000; Fiermonte et al., 1993) and an elevated platelet value in one ET patient have improved to normal levels after treatment (Blaser et al, 2001). However, in 40 ET patients, only the baseline platelet value was reported (Cinar et al, 2021). These alterations in blood parameters—erythrocytosis and thrombocytosis—are correlated with changes in cerebral blood perfusion as measured by mean flow velocities and the detection of MES.

Table 3: Mean flow velocities and Blood parameter values

Author & Year	**Mean flow velocities (cm/s)**		**Hematocrit, %**		**Hemoglobin, g/dl**		**Platelet**	
	Pre-tx	**Post-tx**	**Pre-tx**	**Post-tx**	**Pre-tx**	**Post-tx**		
Fiermonte et al. (1993) [13]	MCA = 39.40 ± 9.34 ACA = 34.05 ± 10.25 PCA = 31.46 ± 5.97 BA = 27.47 ± 7.42	MCA = 47.00 ± 10.85 ACA = 42.10 ± 9.66 PCA = 34.92 ± 5.89 BA = 32.00 ± 5.95	55.78 ± 3.65	46.97 ± 3.45	18.18 ± 0.96	15.44 ± 1.30	N/A	
Del Sette et al. (1995) [10]	MCA_1 = 80 MCA_{14} = 78 MCA_{28} = 80		Hct_1 = 66.1 Hct_{14} = 54.8 Hct_{28} = 49.2		Hb_1 = 23.0 Hb_{14} = 18.4 Hb_{28} = 17.2		**Pre** 300 x $1000/mm^3$	**Post** 311 x $1000/mm^3$
Segura et al. (2000) [11]	**R** MCA_1 = 41 MCA_8 = 43 MCA_{60} = 107 MCA_{120} = 167	**L** MCA_1 = 39 MCA_8 = 40 MCA_{60} = 61 MCA_{120} = 65	Hct_1 = 57 Hct_{60} = 42.5		Hb1 = 19 Hb_{60} = 13.4		234 x10^9/l	350 x10^9/l
Blaser et al. (2001) [12]	N/A		N/A		N/A		682 x10^9/l	*Normal**
Cinar et al. (2020) [14]	**R MCA** Peak-R = 73.4 ± 26.6 EDV-R = 23.7 ± 8.6	**L MCA** Peak-R = 77.5 ± 30.1 EDV-R = 25.7 ± 11	N/A		N/A		436 K/mL** (378-1046)	

Tx: treatment; **MCA:** middle cerebral artery; **ACA:** anterior cerebral artery; **PCA:** posterior cerebral artery; **BA:** basal artery; **R:** right; **L:** left; **Peak**: peak systolic flow velocity, **EDV:** end-diastolic flow velocity
Digits in subscript are days after admission/treatment
** No value specified in the study*
*** Patients detected with MES*

20 subjects from Fiermonte et al.'s study had decreased MFV (MCA = 39.40 ± 9.34) compared to the control group, which significantly improved following treatment (MCA = 47.00 ± 10.85). In another patient, the MFV in the MCA remained elevated in spite treatment (Del Sette et al., 1995). This was explained by the persistent stenosis of the MCA trunk, which was thought to be caused by the migration of clots to the distal branches. One patient had normal basal MFV but subsequently increased on repeat TCD studies (Segura et al., 2000). The authors confirmed the development of stenosis by magnetic resonance angiography (MRA) with absence of flow in the right ICA, and severe stenosis of the proximal right MCA. They hypothesized that this was likely due to microemboli discharge from the carotid siphon, which contributed to the formation of stenosis in the distal MCA. One study did not specify the MFV (Blaser et al, 2001). However, 40 ET patients reported significantly elevated MFV despite treatment compared to the control group (Cinar et al, 2021). The authors explained that high platelet values may form aggregates and cause obstruction by preventing blood cell passage which was subsequently measured as high MFV.

TCD detected MES in four studies (Del Sette et al., 1995; Segura et al., 2000; Blaser et al., 2001; Cinar et al., 2021) with three reporting bilateral findings (Segura et al., 2000; Blaser et al., 2001; Cinar et al., 2021) and one study documenting unilateral MES (Del Sette et al., 1995). A total of 14 patients (22%) had MES monitoring,

showing an average of 132 HITS on the right and 38 HITS on the left in 30 minutes to 1-hour monitoring of MCA. However, the study of Cinar et al. only specified the number of cases with HITS (R-MCA N=8, L-MCA N=5).

Two PV studies repeated MES monitoring and demonstrated a declining trend of HITS (Del Sette et al., 1995; Segura et al., 2000). In contrast to the findings of Del Sette et al., which documented the absence of HITS within the initial month, Segura's study only observed the absence of HITS on the left and 20 HITS per hour on the right MCA on day 60 post-treatment. After a period of four months, no HITS were detected (Segura et al., 2000). Both cases have associated these findings with normalization of blood parameters (hemoglobin 13.4 - 18.4 g/dL and hematocrit 42.5 - 54.8%).

Among the 63 subjects, 3.2% had ischemic stroke and 1.6% had transient ischemic attack with a total of 4.8% stroke risk. Significant improvement, as assessed through clinical evaluation, was observed among the study population after the initiation of treatment. 11 patients (17.5%) became asymptomatic (Segura et al., 2000; Blaser et al., 2001; Fiermonte et al., 1993). Five patients (8%) had a notable decrease in the size of the splenomegaly. Four patients (6%) had persistence of hypertension (Fiermonte et al., 1993); another case had mild right hemiparesis (Del Sette et al., 1995); another had periodic headaches; and another had persistent gouty arthritis (Fiermonte et al., 1993). There was one case with an unvaried outcome (Fiermonte et al., 1993). Clinical improvement was not specified in 40 cases (63%) by Cinar et al.

Table 4 shows the MES monitoring results in the respective studies examining patients with PV and ET. Table 5 and 6 shows the summary of the mean flow velocities and microembolic signals pre- and post-treatment, respectively.

Table 4: MES monitoring results

Author & Year	Cases	MES-Right MCA	MES-Left MCA
Del Sette et al. (1995)	1	recorded per 30 minutes: 0_1 0_{14} 0_{28}	recorded per 30 minutes: 80_1 36_{14} 0_{28}
Segura et al. (2000)	1	recorded per hour: 250_1 360_8 20_{60} 0_{120}	recorded per hour: 30_1 8_8 0_{60} 0_{120}
Blaser et al. (2001)	1	recorded per hour: 14	recorded per hour: 4
Cinar et al. (2020)	11	N=8*	N=5*

MES: Microembolic signals
Digits in subscript are days after admission
**No data regarding number of MES recorded per case*

Table 5: Mean Flow Velocities

		Pre-treatment MFV			Post-treatment MFV	
		Normal	**Decreased**	**Elevated**	**Normal**	**Elevated**
MPN (n= 63)	PV (22 subjects)	1 (1.5%)	20 (31.7%)	1 (1.5%)	20 (31.7%)	2 (3%)
	ET (41 subjects)	-	-	40 (63.5%)	-	-
TOTAL		1 (1.5%)	20 (31.7%)	41 (65%)	20 (31.7%)	2 (3%)

Table 6: Microembolic signals

Cases		Pre-treatment MES	Post-treatment MES
MPN (n= 63)	PV (22 subjects)	2 (3%)	None
	ET (41 subjects)	12 (19%)	None*
TOTAL		14 (22%)	None

**The study of Cinar et al. did not examine post-treatment MES; only the study of Blaser et al. with 1 subject reported absence of HITS after treatment initiation*

An illustrative case of recently diagnosed polycythemia vera manifesting as an acute ischemic stroke with hemorrhagic conversion is depicted in Fig. 2 and 3. TCD exhibited bilateral multiple HITS, which resolved eventually following treatment initiation.

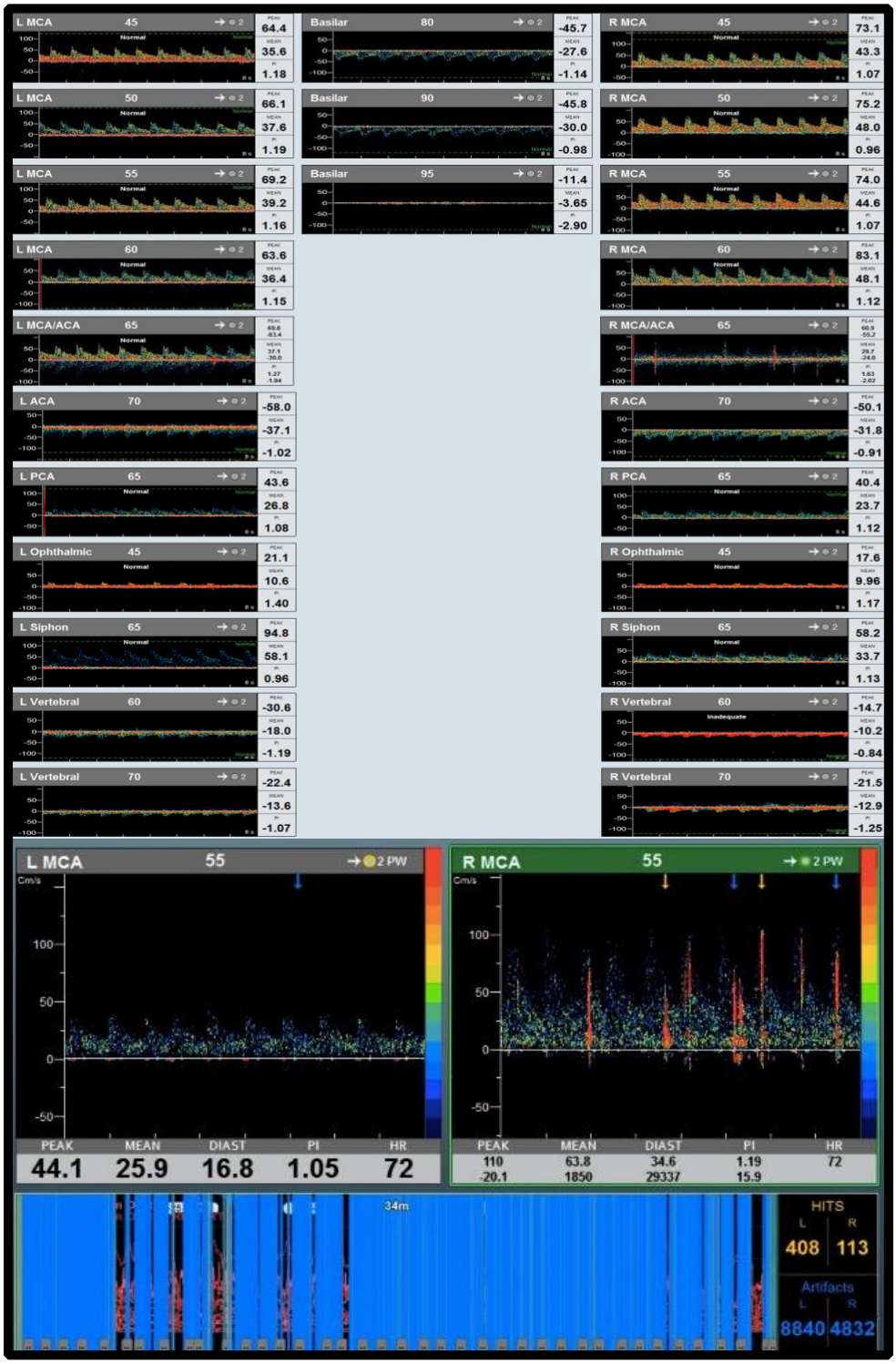

Figure 2: 48-year-old man with headache, left hemiparesis and numbness revealed acute cerebral infarction with hemorrhagic conversion in a background of PV confirmed on genetic testing. TCD showed multiple HITS (Spencer Grade V) on admission with blunted waveform (MFV 35-48 cm/s).

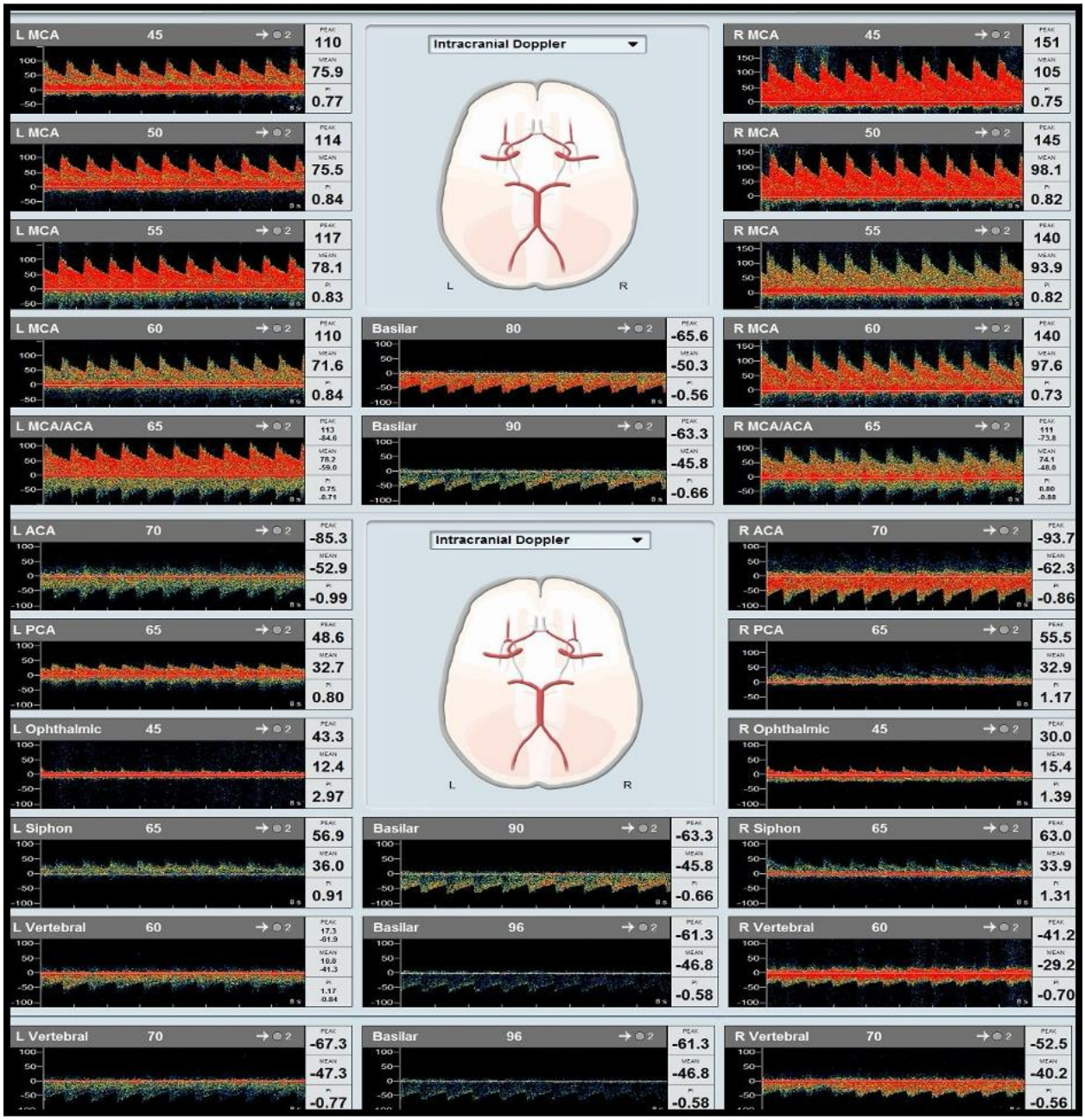

Figure 3: Follow up TCD after 3 months showing normalization of cerebral hemodynamics with MFV 71-105 cm/s. There were no noted HITS on MES monitoring and clinical improvement.

4. Discussion

This systematic review revealed that microembolic signals are common among patients with PV and ET consequent with increased hematocrit, hemoglobin, and platelets. Significant clinical improvement along with improved cerebral blood flow perfusion and absence of MES were observed after treatment initiation and normalization of blood panels. Intracranial stenosis, manifested as increased MFV, developed despite treatment.

The clinical utility of microemboli detection remains uncertain. However, MES has been detected in various potential embolic sources and found to predict stroke risk among patients with acute stroke, symptomatic carotid stenosis, and postoperatively after endarterectomy (King & Markus, 2009). In a meta-analysis, the prevalence of MES was 30% after an acute stroke or TIA, with higher risk of recurrence of cerebral ischemia. It was, however, not linked to poor functional outcomes or mortality (Sudheer et al, 2021). Our review found MES to be numerous

in patients with viscous blood panels that subsequently disappeared following treatment. In one study, MES reappeared after treatment interruption, but the resumption caused the absence of MES and clinical improvement (Blaser et al, 2001). The studies correlated MES detection to formation of microthrombi promoted by increased platelet and red blood cell aggregation, noting that there were no other potential sources of embolism. Thus, MES detection may serve as an indicator of an ongoing asymptomatic cerebral embolization and may be used to assess insufficient secondary stroke prevention.

Two studies of PV patients have documented intracranial stenosis in the background of a hyperviscous blood, as evidence by increased MFV on TCD (Del Sette et al., 1995; Segura et al., 2000). The development of intracranial stenosis among these patients were attributed to their prothrombotic state, causing clot formation, migration and subsequently, stenosis of vessels. An increase in hematocrit was also implicated causing endothelial dysfunction by reducing endothelial surface thickness, thereby modulating inflammation, permeability, and atherosclerosis formation (Richter et al., 2011).

Jak2VF mutation also contributes to thrombosis, as reported by Wang et al. where its expression in hematopoietic cells promotes the development of atherosclerosis at a faster rate, characterized by unstable plaques. This result is consistent with the higher incidence of atherothrombotic cardiovascular disease that has been observed in patients with clonal hematopoiesis or MPN associated with JAK2VF (Wang et al., 2018).

TCD may be used to monitor the effects of therapeutic interventions in PV and ET patients, as exhibited by this review. By tracking changes in cerebral blood flow dynamics and detection of MES, clinicians can gauge the cerebrovascular health of MPN (PV and ET) patients and make diagnostic and prognostic assessments based on these trends.

Limitations of the review include the lack of randomized trials and other observational studies with larger sample sizes to assess the practicability of TCD in monitoring PV and ET. Further, there are limited studies available that assess MPN with TCD using recent and more advanced technology, as the studies included in the review were dated two decades prior to the composition of this systematic review. For future studies, the authors recommend a standardized protocol for TCD examination, which includes monitoring at baseline, specific time frame post-treatment, and follow-up for uniform data reporting.

5. Conclusion

The review elucidates that while TCD is not a primary diagnostic tool for PV and ET, it can be practical and valuable in the context of monitoring cerebrovascular complications, assessing thrombotic risk, evaluating treatment responses, and conducting research related to these myeloproliferative diseases. Prognostically, it also enables clinicians to make informed predictions about the patient's future risk of cerebrovascular events and provides an opportunity for individualized risk assessments and treatment planning. However, TCD should be used as part of a comprehensive diagnostic and monitoring approach alongside other clinical and laboratory assessments. To enhance the validity of the present study, a larger study population among these patients are recommended in future research.

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Conflict of Interest: The authors declare no conflict of interest.

Informed Consent Statement/Ethics Approval: Not applicable.

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