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Message

On the Formulation of the First-Ever Mechanical Thrombectomy Guideline in Pakistan.

I am deeply honoured to announce the formulation of Pakistan's inaugural national guideline on Mechanical Thrombectomy, a significant milestone in the advancement of stroke care in our country. This initiative reflects our unwavering commitment to providing state-of-the-art medical treatment to all citizens, in line with global best practices.

Mechanical Thrombectomy is a highly effective procedure for treating acute ischaemic stroke, and its successful implementation requires a clear, standardized framework to ensure consistency, quality, and patient safety. This guideline has been developed with the collaborative efforts of leading experts in neurology, interventional radiology, neurosurgery, and stroke care, ensuring that it addresses the unique needs and challenges of our healthcare system.

The formulation of this guideline marks a new chapter in stroke management in Pakistan. It will serve as a critical tool for healthcare professionals across the country, offering them evidence-based protocols for timely diagnosis, appropriate patient selection, and the optimal use of thrombectomy techniques. This is a step forward in reducing stroke-related morbidity and mortality, especially in cases where time is of the essence.

I extend my gratitude to all the experts, contributors, and institutions involved in this groundbreaking work. Their dedication to advancing healthcare in Pakistan has paved the way for improved outcomes in stroke patients.

Together, we are strengthening the foundation for a future where access to cutting-edge stroke treatment.

Sincerely,
Dr Nadeem Fazal
MBBS, FRCP(Edinburgh),FRCP(Glasgow),
FCPS(Medicine)
Professor of Medicine
Dean Medicine and Allied,National University of Medical
Sciences, Rawalpindi

Message

On the Formulation of the First-Ever Mechanical Thrombectomy Guideline in Pakistan

It is with immense pride and great responsibility being part of the team for completion of Pakistan's first-ever national guideline on Mechanical Thrombectomy, an advanced and life-saving procedure for patients suffering from acute ischemic stroke. This is a landmark achievement for the medical community of our nation, as we move towards setting new standards in stroke care.

The formulation of this guideline is a testament to the dedication of the interdisciplinary team of experts, including neurologists, interventional radiologists, neurosurgeons, and other healthcare professionals. Their collaborative efforts have resulted in a comprehensive and practical guide tailored to the specific healthcare challenges and needs of Pakistan.

Mechanical Thrombectomy has proven to significantly improve outcomes in patients with large vessel occlusion strokes, particularly when performed within a critical time window. With this national guideline, we aim to standardize its implementation across the country, ensuring that healthcare providers have the necessary tools and protocols to deliver timely and effective treatment.

I am confident that this guideline will not only improve stroke outcomes but will also inspire further advancements in neuro-intervention across Pakistan. I would like to express my sincere appreciation to all who contributed their expertise and efforts in shaping this pioneering document. Your work has laid the foundation for a future where mechanical Thrombectomy becomes a routine and accessible part of stroke care, benefiting countless lives.

Together, we are building a stronger healthcare system, ensuring that the people of Pakistan receive the very best in medical care.

Sincerely,
Dr Syed Farrukh Nadeem,
MBBS,FCPS(Diagnostic Radiology)
Professor of Radiology, National University of Medical Sciences (NUMS)
Rawalpindi.

Message

It is a moment of great pride and fulfillment to witness the successful formulation of Pakistan's first-ever national guideline on Mechanical Thrombectomy. This initiative marks a significant breakthrough in stroke management in Pakistan and opens new avenues for improving patient outcomes in cases of acute ischaemic stroke.

At Lahore General Hospital, where first stroke center was established. we have seen firsthand the devastating effects of stroke and the critical need for timely, effective intervention. Mechanical Thrombectomy, as an advanced neuro-interventional procedure, offers hope to patients who otherwise faced limited treatment options. This new guideline will serve as a vital tool in ensuring that healthcare providers across the country can implement this life-saving procedure with precision and consistency.

The creation of this guideline reflects the dedication, collaboration, and hard work of an outstanding team of experts from across disciplines. Interventional Neuro-radiologists, neurologists and neurosurgeons have come together to create a standardized, evidence-based approach that will pave the way for more timely diagnosis and appropriate patient selection. It is a step toward ensuring that every eligible stroke patient in Pakistan has access to the best possible care, regardless of their location.

I am deeply honoured to be part of this important national achievement. I believe this guideline will not only enhance our ability to treat stroke patients but also promote the growth and development of neuro-intervention as a field in Pakistan. I extend my heartfelt thanks to all the contributors for their relentless efforts and vision. Together, we are shaping the future of stroke care in our country.

Sincerely,
Prof. Umair Rashid Chaudhary
Head of Department of Neuro-Radiology & Interventional Neuroradiology, Lahore General Hospital
On the Formulation of the First-Ever Mechanical Thrombectomy Guideline in Pakistan
MBBS, DPH, DMRD, MCPS, M.Sc. Neurovascular Diseases,
European Diploma in Intervention Neuroradiology

Message

It is a matter of immense pride and professional fulfillment to have contributed to the formulation of Pakistan's first-ever mechanical thrombectomy guidelines. Stroke remains a significant cause of morbidity and mortality in our region, and mechanical thrombectomy represents a groundbreaking treatment modality that has proven to significantly improve outcomes for stroke patients. Formulation of these guidelines is an excellent example of inter-speciality collaboration.

Being part of the dedicated team of experts that developed these guidelines has been a rewarding experience. Our collective effort reflects a committment to advancing the standard of care and ensuring evidence-based practices tailored to our healthcare infrastructure and patient needs.

I am confident that these guidelines will serve as a beacon of light for clinicians across the country, enabling timely and effective intervention for stroke patients and ultimately saving countless lives. This milestone is just the beginning, and I look forward to continued collaboration in shaping the future of stroke care in Pakistan."

Sincerely,
Dr. Asim Javed
MBBS,MRCP(UK),MRCP(Glasg), FCPS, FSCAI(USA),
Fellowship in Interventional Cardiology (UK),
ESMINT Stroke Diploma / WIST Certified Stroke Interventionist,
Consultant Interventional Cardiologist,
Head of Cardiology Department & Director Stroke Program,
Rawalpindi Institute of Cardiology, Rawalpindi

GUIDELINE

Guidelines for Mechanical Thrombectomy in Acute Stroke in Pakistan

Guideline-Driven, Practical, and Scenario-Based Approaches for Acute Ischaemic Stroke Intervention– Pakistan

Khawaja Muhammad Baqir Hassan[1], Umair Rashid Chaudhary[2], Asim Javed[3], Sohail Akhtar[4], Asif Hashmat[5], Tathir Baqir Hassan[6], Raza Rahim Hyder[7]

Background: Acute ischaemic stroke (AIS) is one of the leading cause of mortality and morbidity. Recent developments in the treatments option such as intravenous thrombolysis and Endovascular therapy(EVT) or mechanical thrombectomy(MT) have significantly changed the clinical outcome in these patients.[1] The EVT is dependent on many variables such as last known well (LKW), NIHSS score, Plain CT Brain ASPECT score(CT-ASPECT), type of vessel, early versus late window of presentation(0-6 hours vs 6-24 hours), Estimation of core volume by advance imaging (CT perfusion or MR Perfusion), age, gender and co-morbids.[2] Many trials have also been conducted on these various variables and their favourable / adverse effects on clinical outcome in terms of Modified Rankin scale(MRS).[3]

Aim: To develop a consensus among the various centers in Pakistan providing EVT in AIS with standard and rationalized treatment to attain uniform and sustainable results in the direction of international guidelines, various Randomized clinical trials and meta-analysis.

Objective: A documented guideline for Pakistani neuro-interventionists and physicians providing services to the patients of AIS by EVT.

Methodology: International guidelines by American heart associations (AHA-USA) and national health system (NHS-UK), Randomized Control Trials (RCT) and clinical studies already published were studied and formulated as basis of these approaches. These guidelines and RCT form the cardinal basis of the ischaemic stroke intervention practiced mainly in USA and United Kingdom. Neuro-interventionist from five major hospitals including Armed Forces Institute of Radiology & Imaging, Rawalpindi (AFIRI), Pak Emirates Military Hospital (PEMH), Rawalpindi, Rawalpindi Institute of Cardiology (RIC), Lahore General Hospital, Lahore (LGH) and Combined Military Hospital, Lahore (CMH) were involved in formulation of the guidelines. Minimum clinical experience of each Interventional Neuro-Radiologist And Neuro-Interventionist was 25 MT performed independently, attended minimum of 100 stroke codes in a calendar year consecutively for the last two years. All the Neuro-interventionist of these major stroke centers across the country, practicing and performing mechanical thrombectomies, carefully studied and discussed each scenario. In addition to these inputs from neurologist of these hospitals and public health department of army was also consulted.

Operational definitions, individual clinical scenario based on type and size of vessel and summary on the basis of recommendations were devised for local practice. Selection / Inclusion criteria of each patient was devised on the basis of international guidelines and RCT keeping in view the local resources, financial status and health care facilities available in the hospitals. Initial selection of the possible candidate for MT was based on cutoff of LKW on 6 hour window. Before 6hour was mainly based on NHS/AHA guidelines and extended window on DAWN/DIFFUSE trials. Once selected, approach for individual vessel and clinical situation was devised.

Operational Definitions

Primary Operator: A doctor who has received formal training in intervention of Acute Ischaemic stroke and has attained the desired level of competency of performing

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the procedure and handling the complications.[4,5]

Secondary Operator: A doctor who has assisted / under going training for acute ischaemic stroke intervention in a level-1 hospital for stroke Intervention under the supervision of a senior primary operator.[6]

Level 1 Stroke Centre / Hospital: An acute ischaemic stroke related service provider hospital that has the full spectrum of neuro-intervention, acute ischaemic stroke including tPA and mechanical thrombectomy, minimal referral of 250 patients per year and performing at least 50 thrombectomies in a year.[7]

Level 2 Stroke Centre / Hospital: An acute ischaemic stroke related service provider hospital that offer endovascular therapy for acute ischaemic stroke in the form of mechanical thrombectomy with tPA services and, minimal referral of 100 patients per year and performing at least 50 thrombectomies in a year.[7]

Large Vessel: Intracranial vessel having diameter more than 2.0 mm.[8]

Includes:

1. Internal Carotid Artery
2. Middle cerebral Artery M1 segment (MCA – 2.7mm±0.2mm)
3. Basilar Artery (BA – 3.2mm ± 0.2mm)
4. Vertebral Artery (VA – 2.8mm ± 0.2mm)[9]
5. Dominant side M2 segment of MCA if diameter >2.0mm[9]

Medium Vessel: Intracranial vessel having diameter of 0.75mm-2.00mm.[9]

Includes:

1. M2 segment of dominant MCA if <2.0mm and M2 segment of non-dominant side.[9]
2. Anterior cerebral arteries (ACA)
3. Posterior Cerebral arteries (PCA)

Small Vessel: Intracranial vessel having diameter less than 0.75mm.[8,9]

Last Known well (LKW): The last known time when the patient was seen normal

Wake up stroke: Went to sleep normally and woke up with symptoms of stroke.

Anterior Circulation: Includes ICA, MCA and ACA vessels

Posterior Circulation: Includes VA, BA and PCA.

Extended Window period: 06-24 hours of LKW

Proximal segment of M2 segment of MCA: Horizontal segment of M2 right after bi/tri furcation of the M1 segment of MCA.

High Intra-cranial ICA Isolated Occlusion: ICA Occlusion distal to cavernous portion

BMM: Best Medical Management

Selection Criteria

Selection Criteria for Anterior Circulation AIS for Mechanical Thrombectomy (based on plain CT brain and CTA)[10,11]

LKW = ≤06 hours
Plain CT ASPECT Score = ≥6
NIHSS = ≥6 or less than 6 with disabling stroke
LVO present
Age = ≥18 years up to 80 years
Pre stroke mRS = 0 or 1

Extended Window Criteria for Anterior Circulation AIS for EVT / MT (based on additional advance imaging CTP brain and MRI)

LKW = 06-24 hours
DAWN / DIFFUSE-3 inclusion criteria.[12]
Radiological Evidence of Salvageable brain parenchyma

Eligibility Criteria for Extended window

DAWN12
LKW 6-24
LVO

Radiological evidence of salvageable brain
DAWN/DEFUSE eligibility criteria
CTP- core less than 70ml, penumbra > 15ml, Penumbra: Core Ratio >1.8

Eligibility Criteria for Posterior circulation

Selection Criteria for Posterior Circulation AIS for Mechanical Thrombectomy (based on plain CT brain and CTA) when LKW ≤6 hours

LKW = ≤06 hours
Plain CT pcASPECT Score = ≥6
NIHSS = ≥6 or less than 6 with disabling stroke
LVO present
Age = ≥18 years up to 80 years
Pre stroke mRS = 0 or 1

Selection Criteria for Posterior Circulation AIS for Mechanical Thrombectomy when LKW ≥6- 24 hours – Extended Window (based on plain CT brain, CTA and plain MRI Brain – DWI/FLAIR/T2WI Mismatch) LKW ≥ 06 – 24 hours

MRI Brain DWI/FLAIR/T2WI sequences specifically for viability of brain stem (Most important)

Plain CT pcASPECT Score = ≥6
NIHSS = ≥6 or less than 6 with disabling stroke
LVO present
Age = ≥18 years up to 80 years
Pre stroke mRS = 0 or 1

Various clinical scenarios have been individually discussed in subsequent tables for better understanding and simplification of the complex procedural decision making. Tables 1-9 outline these situations, specifically divided on the basis of type of vessel involved and LKW of the patient. Each table includes standard parameters critical in selection of the patient for mechanical thrombectomy. These parameters are age, pre=stroke mRS, LKW, NIHSS, imaging including plain CT brain, advance imaging (CTP brain and CTA Head & Neck) and MRI brain. Brief description of the concerned guideline is also given under the table as well. These tables discuss the individual scenario under the influence of the international guidelines. The clinical scenarios have been broadly classified into anterior and posterior circulations. Table 1 to 7 describe most frequently encountered anterior circulations whereas 8 to 9 summarises that of posterior circulation.

Table -1: Clinical Situation-1

Middle Cerebral Artery – M1 Segment[13]					
Age in Years	**Pre-Stroke mRS**	**LKW**	**NIHSS**	**CT ASPECT**	**IV Thrombolysis**
18-80	0-1	≤06 hours	≥6	≥6	Given/Not Given(14)

mRS = Modified Rankin Scale, LKW = Last known well,NIHSS=National Institute of Health Stroke Scale, ASPECT = Alberta Stroke Early Computed Tomography, IV = Intra-venous

Table-1 describes consensus and protocols that have been developed for mechanical thrombectomy in M1 segment of the MCA. As per AHA / ESO / UK & Ireland guidelines for acute ischaemic stroke, eligible patients will receive EVT for M1 occlusion despite the fact tPA was given or not.[15]

Table-2 shows scenario where extended window upto 24 hours M1-middle cerebral artery occlusion is present with good CT-ASPECT. As Per DIFFUSE-3 trial, CT-ASPECT in extended window can be ≥3 or more, but considering the facilities and resources in our setup, we suggest CT-ASPECT ≥5 with radiological evidence of significant salvageable brain as seen on CTP brain.

Table-2: Clinical Situation -2

Middle Cerebral Artery – M1 Segment – DEFUSE -3 Criteria[12]							
Age in Years	**Pre-Stroke mRS**	**LKW**	**NIHSS**	**CT ASPECT**	**CTP/DWI/FLAIR**	**Core Infarct Volume**	**Penumbra Infarct core ratio**
18-80	0-1	6-24 hours	>6	≥5	Salvageable brain tissue / Mismatch	<70ml	≥1.8

mRS = Modified Rankin Scale, LKW = Last known well,NIHSS=National Institute of Health Stroke Scale, ASPECT = Alberta Stroke Early Computed Tomography, IV = Intra-venous

Table-3: Clinical Situation -3

Middle Cerebral Artery – M1 Segment – DAWN Criteria[12]						
Age in Years	**Pre-Stroke mRS**	**LKW**	**NIHSS**	**CT ASPECT**	**CTP/DWI/FLAIR**	**Core Infarct Volume**
>80	0-1	6-24 hours	>10	≥5	Salvageable brain tissue / Mismatch	<21ml

mRS = Modified Rankin Scale, LKW = Last known well,NIHSS=National Institute of Health Stroke Scale, ASPECT = Alberta Stroke Early Computed Tomography, CTP= Computed tomography perfusion,, DWI=Diffusion weighted imaging, FLAIR=Fluid attenuated inversion recovery,ml = milliliter.

Table – 3 shows patients above 80 years and as by DAWN trial, patients having age of 80 or more years should meet the above criteria when presenting in extended window. Counselling of the family and assessment of the local facilities and logistics are also vital in this case.

Table – 4 reveals the criteria of selection of candidates for medium vessel occlusion. By HERMES meta-analysis, proximal segment of M2 of dominant MCA should be

Table-4: Clinical Situation -4

Middle Cerebral Artery – M2 Segment – Dominant[16,17]						
Age in Years	**Pre-Stroke mRS**	**LKW**	**NIHSS**	**CT ASPECT**	**CTP/DWI/FLAIR**	**Segment Diameter >2.0mm**
18-80	0-1	<6hours	>10	≥6	Salvageable brain tissue / Mismatch	Proximal Segment

mRS = Modified Rankin Scale, LKW = Last known well,NIHSS=National Institute of Health Stroke Scale, ASPECT = Alberta Stroke Early Computed Tomography, IV = Intra-venous, CTP = Computed tomography perfusion, DWI = Diffusion weighted imaging, FLAIR = fluid attenuated inversion recovery.

Table-5: Clinical Situation -5

Isolated Proximal Extra-cranial Internal Carotid Artery with fair Contra lateral flow[18–20]							
Age in Years	**Pre-Stroke mRS**	**LKW**	**NIHSS**	**CT ASPECT / CTA**	**CTP/DWI/FLAIR**	**Segment**	**BP Augmentation**
18-80	0-1	<6hours	>10 or Disabling stroke	≥6 / fair collaterals	Salvageable brain tissue / Mismatch	Isolated Proximal extracranial ICA occlusion	In-effective

mRS = Modified Rankin Scale, LKW = Last known well, NIHSS=National Institute of Health Stroke Scale, ASPECT = Alberta Stroke Early Computed Tomography, CTA = Computed tomography angiography, CTP= Computed tomography perfusion,, DWI=Diffusion weighted imaging, FLAIR=Fluid attenuated inversion recovery, ICA = Internal carotid artery

attempted if advance imaging and above mentioned eligibility criteria are met. As no definite Guideline, RCT or meta-analysis exist on the significance of non-dominant or dominant distal M2 EVT the BMM should be practiced as per UK & Ireland Stroke guidelines 2023.[15]

Table – 5 describes the clinical scenario for isolated extra-cranial internal carotid artery occlusion. No randomized controlled trial (RCT) has been conducted on this topic to date. The incidence of complications in this specific scenario is notably high. According to studies,[17] the rate of immediate asymptomatic haemorrhage is lower, and revascularization rates are higher compared to ICA tandem occlusion with endovascular treatment (EVT) involving mechanical thrombectomy (MT) and extracranial internal carotid artery (ICA) stenting. However, it's important to note that the occurrence of symptomatic hemorrhage within 30 days was considerably higher than with EVT for ICA tandem occlusion.[17,18] Additionally, the incidence of all types of strokes within 30 days is similar, and the functional outcome at 90 days (measured by modified Rankin Scale, mRS) is significantly poorer (42.4% vs. 49.6%) than with EVT for tandem occlusion.[18]

EVT yields subpar functional outcomes in this particular clinical setting. In addition, when considering factors such as local resources, medical facilities, time to emergency room (ER), time to femoral puncture, logistical challenges, patient response, and compliance post-EVT, it is expected that the functional outcome would be even worse in revascularization of isolated internal carotid artery (ICA) occlusion compared to what is reported in Western literature. Furthermore, there is a lack of guidelines, randomized controlled trials (RCTs), or meta-analyses available for this specific scenario.

Hence, proceeding with EVT management for isolated proximal (Extracranial) ICA complete occlusion is linked to a high rate of complications and poor clinical outcomes, and therefore, it should be avoided. It is imperative to communicate this information to the patient's attendants as well.

Table – 6 describes the clinical scenario of ICA terminus occlusion with poor or minimal contra-lateral flow to ipsilateral MCA.No randomized controlled trial (RCT) has

Table-6: Clinical Situation -6

Isolated Distal Intra-cranial (Supra-cavernous to terminus) Internal Carotid Artery Occlusion with No / poor Contra lateral flow[18]							
Age in Years	**Pre-Stroke mRS**	**LKW**	**NIHSS**	**CT ASPECT / CTA**	**CTP/DWI/FLAIR**	**Segment**	**Ischemic Core**
<60 years	0-1	<6hours	>6 or Disabling Stroke	≥6 / Poor collateral	Salvageable brain tissue / Mismatch	Supra-cavernous intracranial ICA occlusion	<70ml Mismatch volume >40ml

mRS = Modified Rankin Scale, LKW = Last known well, NIHSS=National Institute of Health Stroke Scale, ASPECT = Alberta Stroke Early Computed Tomography, CTA = Computed tomography angiography, CTP= Computed tomography perfusion,, DWI=Diffusion weighted imaging, FLAIR=Fluid attenuated inversion recovery, ICA = Internal carotid artery

explored this topic to date, highlighting the notably high incidence of complications in this specific scenario, particularly in the younger age group. However, it's crucial to consider that younger individuals tend to have relatively better clinical outcomes, as noted in some studies.[17,18] According to these studies, endovascular treatment (EVT) for intracranial internal carotid artery (ICA) occlusion (supra-cavernous to terminus, with no or fair anterior cerebral artery (ACA) or middle cerebral artery (MCA) opacification) shows slightly better functional outcomes.[17,18,21]

While the rate of immediate asymptomatic hemorrhage is lower and revascularization rates are higher compared to ICA tandem occlusion with EVT involving mechanical thrombectomy (MT) and extracranial ICA stenting, the occurrence of symptomatic hemorrhage within 30 days was considerably higher in ICA tandem occlusion.[17,18] Additionally, the incidence of all types of strokes within 30 days is similar, and the functional outcome at 90 days (measured by modified Rankin Scale, mRS) is significantly poorer (42.4% vs. 49.6%) compared to EVT for tandem occlusion.[18]

Although EVT may yield subpar functional outcomes in this clinical setting, when considering factors such as local resources, medical facilities, time to emergency room (ER), time to femoral puncture, logistical challenges, patient response, and compliance post-EVT, it is anticipated that the functional outcome would be even worse in revascularization of isolated internal carotid artery (ICA) occlusion compared to what is reported in Western literature. However, due to the lack of guidelines, RCTs, or meta-analyses for this specific scenario, proceeding with EVT management for isolated distal (intracranial) ICA complete occlusion with poor or non-opacification of ACA/MCA or both is still considered a better option than best medical management (BMM) in younger individuals, albeit with a high rate of complications and poor clinical outcomes.

Therefore, attempting EVT in such cases is recommended, but it is crucial to communicate this information effectively to the patient's family.

Table-7 shows criteria for tandem occlusion. Tandem occlusion trial TITAN is still awaited. Therefore the management varies from patient to patient. No consensus has been developed on choice of treatment, treatment strategy and regime of dual anti-platelets.[23] The decision of EVT lies with the INR and clinical analysis of the situation.

Table – 8 describes eligibility criteria of posterior circulation large vessel occlusion. IVT & EVT in posterior circulation are administered on ASAP basis, however the recent ATTENTION trial has demonstrated that NIHSS >10 and LKW <12 has the best functional outcome (mRS @ 90 days) when compared to BMM.

Table – 9 describes the isolated vertebral artery occlusion. Solitary vertebral artery occlusion management is based on cause of occlusion, site of PICA especially if dissection is present.[25] It will be treated on emergent basis and as per same protocol of Posterior circulation occlusion with addition of the management of dissection.

Table-7: Clinical Situation -7

Tandem Occlusion Internal Carotid Artery[22,23]						
Age in Years	**Pre-Stroke mRS**	**LKW**	**NIHSS**	**CT ASPECT / CTA**	**CTP/DWI/FLAIR**	**Segment**
<50 years	0-2	<8hours	>6 or Disabling Stroke	≥6 / Poor collateral	Salvageable brain tissue / Mismatch	extracranial ICA stenosis ≥ 90% and Intracranial LVO

Table-8: Clinical Situation -8

Vertbero-Basilar Artery &/Or PCA Occlusion[24]						
Age in Years	**Pre-Stroke mRS**	**LKW**	**NIHSS**	**CT pcASPECT / CTA**	**CTP/DWI/FLAIR**	**Artery/Segment**
<80 years	0-2	<12hours	>10 or Disabling Stroke	≥6 / fair/Poor collateral	Salvageable brain tissue / Mismatch	Basilar Artery Any

mRS = Modified Rankin Scale, LKW = Last known well, NIHSS=National Institute of Health Stroke Scale, pcASPECT = posterior circulation Alberta Stroke Early Computed Tomography, CTA = Computed tomography angiography, CTP= Computed tomography perfusion,, DWI=Diffusion weighted imaging, FLAIR=Fluid attenuated inversion recovery, ICA = Internal carotid artery

Table-9: Clinical Situation -9

Solitary Vertebral Artery Occlusion[24]						
Age in Years	**Pre-Stroke mRS**	**LKW**	**NIHSS**	**CT pcASPECT / CTA**	**CTP/DWI/FLAIR**	**Artery/Segment**
<80 years	0-2	<12hours	>10 or Disabling Stroke	≥6 / fair/poor collateral	Salvageable brain tissue / Mismatch	Intra cranial

mRS = Modified Rankin Scale, LKW = Last known well, NIHSS=National Institute of Health Stroke Scale, pcASPECT = posterior circulation Alberta Stroke Early Computed Tomography, CTA = Computed tomography angiography, CTP= Computed tomography perfusion,, DWI=Diffusion weighted imaging, FLAIR=Fluid attenuated inversion recovery, ICA = Internal carotid artery

Note: Recommendations adopted from Guidelines for the Early Management of Patients with Acute Ischaemic Stroke: 2019 Update.[7]

- Class of recommendation (Class): I (strong benefit), IIa (moderate benefit), IIb (weak benefit), III (moderate no benefit or strong harm)
- Level of evidence (LOE): A (high quality), B-R (moderate quality randomized), B-NR (moderate quality nonrandomized), C-LD (observation or registry with limited data), C-EO (expert opinion).

Discussion

In early days hyper acute stroke or acute stroke was treated conservatively. Then systemic thrombolysis or IV thrombolysis by alteplase (tPA) revolutionized the treatment. But altelplase (tPA) administration is chiefly time bound and effective for small vessels.[26,27] In early years of 21st century, use of aspiration or physical removal of clot by mechanical devices was introduced.[28] In initial days the success was limited, but with introduction of better aspiration catheters, improved navigation techniques and use of new mechanical devices such as intra-cranial stent retrievers, revolutionized the scope of MT.29 Now the intravenous tPA, MT alone or combined have become the standard treatment of the hyper-acute or acute ischaemic stroke.[4] This new specialty is also gaining popularity and momentum in Pakistan. However the selection and decision of when and how to treat the patient depends upon many variables. Time of presentation, age, comorbidities and type of vessel involved are the main parameters of decision making. However in our country the availability of health care facilities and financial status also play an important role.

Currently, the selection of disposables and patient eligibility for mechanical thrombectomy (MT) is largely dictated by the individual preferences of the primary operator. The decision-making process, including patient selection and procedural planning, rests predominantly with the lead interventionalist. However, we believe that this document can serve as a critical step toward achieving uniformity and standardization in these practices. By establishing structured guidelines, we aim to enhance procedural consistency, optimize resource utilization, and ultimately improve patient outcomes.

Additionally, it is crucial to define both the qualifications required to perform MT and the appropriate healthcare settings for its execution. According to international guidelines, mechanical thrombectomy for acute stroke should only be performed in designated stroke centres that meet Level 1 or Level 2 hospital criteria. These centres must be equipped with the necessary infrastructure and personnel, including both primary and secondary operators trained in neurointervention. Establishing these criteria ensures that MT is conducted in a controlled and high-quality environment, thereby maximizing the efficacy of stroke intervention and reducing procedural variability.

Each patient is a different case. Similar clinical situation in two different patients warrants different clinical approach and decision making strategy. The major component of successful procedure and favorable clinical outcome is the correct decision. Two major parts of a successful procedure are documented, angiographic success and improvement in mRS of the patient. It has been observed over due course of time and through the clinical experience of the various centers and neuro-interventionists that the decision of selection of patients, approach and choice of disposables play the pivotal role in successful recanalization of the vessel and improvement of stroke related 90 day mRS of the patient. Many times angiographic success is achieved, however the patient does not improve clinically or significant morbidity is encountered. Another important aspect is the financial and resource burden. The health care facility providing services to such patients needs critical care setups for these patients. In western setups facilities and financial resources are planned such that no burden is born by the patients. But in our country, mostly it is the patient's family that is bearing the cost of the treatment.

Mechanical thrombectomy and it's after care are an expensive treatment in Pakistan. This also formulates an important component of decision making and

Table 10 describes the current international recommendation with class and level of evidence for various clinical situations.

Table-10: Recommendations for Mechanical Thrombectomy Indications.[13]

Class	LOE	Recommendation
I	A	0 to 6 Hours from Onset 1. Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (i) prestroke mRS score of 0 to 1; (ii) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (iii) age ≥18 years; (iv) NIHSS score of ≥6; (v) ASPECTS of ≥6; and (vi) treatment can be initiated (groin puncture) within 6 hours of symptom onset.
IIb	B-R	2. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for carefully selected patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who: a. have causative occlusion of the MCA segment 2 (M2) or MCA segment 3 (M3) portion of the MCAs b. have prestroke mRS score >1, ASPECTS <6, or NIHSS score <6, and causative occlusion of the internal carotid artery (ICA) or proximal MCA (M1)
IIb	C-LD	c. have causative occlusion of the anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries
I	A	3. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended
IIa	B-R	4. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable

LOE = Level of evidence, mRS = Modified Rankin Scale, LKW = Last known well, NIHSS=National Institute of Health Stroke Scale, AIS = Acute ischemic stroke, MCA = middle cerebral artery, pcASPECT = posterior circulation Alberta Stroke Early Computed Tomography, CTA = Computed tomography angiography, CTP= Computed tomography perfusion,, DWI=Diffusion weighted imaging, FLAIR=Fluid attenuated inversion recovery, ICA = Internal carotid artery

counselling. The approximate cost of the MT with hospital admission for an individual or organization is same. At present exchange rate approximate cost of MT varies from 0.8 to 1.2 million pak rupees. Another 300- 450 thousands rupees are added if extra or intra-cranial angioplasty and stenting is added. Although this cost is not important when lifelong morbidity and dependency of the patient are taken into account. Furthermore the slow and cumulative cost of the patient care, dependency, recurrent admissions and physiotherapy are more than what is spent on MT. It is in addition to the mental stress of the individual and the family.

To minimize the aforementioned variables it was the need of the time to standardize the hyper acute ischemic stroke treatment for better clinical outcome and judicial use of resources. Therefore these initial guidelines were formulated by the neuro-interventionist of Major stroke centers in Pakistan.

Conclusion

These scenario based guidelines will help the neuro-interventionist, stroke neurologists and neuro-radiologists to standardize, rationalize and justify the Mechanical Thrombectomy in Pakistan.

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Abbreviations:

ACA = Anterior cerebral artery
AIS = Acute Ischemic Stroke
ASPECT = Alberta Stroke Program Early Computed

Table 11 describes the consolidated summary of all the clinical situations with main focus on guideline, recommendation and suggestion in terms of remarks for the purpose of quick reference and early decision making.

Table-11- SUMMARY

Ser	PICO	Guideline	Recommendation	Remarks
1	18-80 years, LVO(M1/Intracranial ICA), LKW < 4.5 hrs., NIHSS>6, CT Aspect>6	tPA & MT indicated.	Established and clearly defined guideline. Should be performed in our setup.	Although very less number of patients present in our setup in this window, but MT should be performed in these patients despite tPA is given.
2	18-80 years, LVO (M1/Intracranial ICA), LKW > 4.5 hrs. -12 hours, NIHSS>6, CT Aspect>6, CTA good collaterals, CTP evidence of salvageable brain	MT Indicated	Proceed with MT as Established and clearly defined guideline	Most of the patients in out setup present in this time frame. MT should be performed. If unable to perform CT perfusion, then do DWI/FLAIR/T2WI MRI, assess clinically and proceed with MT
3	18-80years or > years, LVO(M1/Intracranial ICA), LKW > 12-24 hours, NIHSS>6, CT Aspect>3-5, CTA fair collaterals, equivocal CTP evidence of salvageable brain	Selected number of patients under go MT	In our setting, a substantial number of patients present during this period. It's important to take into account comorbidities, available medical resources, and logistical considerations for both the organization and the patient. Mechanical thrombectomy (MT) may be considered for patients who meet the eligibility criteria outlined in the DAWN or DIFFUSE-3 trials as described in Scenarios 2 and 3.	Medical facilities, financial constraints and post MT care of these patients puts significant burden on both the healthcare system and the family of the patients. No data on 90day mRS is available in local population to provide strong evidence of benefit of MT in these patients. Hence, the eligibility criteria for DAWN & DIFFUSE-3 should be strictly applied with prior consent and counseling of the family.
4	18-80 years, LVO(M1/Intracranial ICA), LKW < 4.5 hrs., NIHSS<6 (Disabling stroke), CT Aspect>6	tPA & MT indicated.	Established and clearly defined guideline. Should be performed in our setup.	Although very less number of patients present in our setup in this window, but MT should be performed in these patients despite tPA is given.
5	18-80 years, LVO (M1/Intracranial ICA), LKW > 4.5 hrs. -12 hours, NIHSS<6, Disabling stroke, CT Aspect>6, CTA good collaterals, CTP evidence of salvageable brain	MT Indicated	Proceed with MT as Established and clearly defined guideline	Most of the patients in out setup present in this time frame. MT should be performed. If unable to perform CT perfusion, then do DWI/FLAIR/T2WI MRI, assess clinically and proceed with MT
6	18-80years, LVO(M2 > 2.0mm) or MVO(M2 of either side) LKW > 4.5-24 hours, NIHSS>6, CT Aspect>6, CTA fair collaterals, CTP evidence of salvageable brain	tPA ± MT in proximal M2 with stent retriever	Only attempt to treat the dominant proximal segment of the M2 with EVT, if its caliber is greater than 2.0mm, if the patient has an NIHSS score of greater than 10, a CT ASPECT score of at least 6, radiological evidence indicating salvageable brain tissue, and there are no contraindications to tPA or the procedure.	The eligibility criteria for these patients must be strictly adhered to, as using a stent retriever for MVO could upset the risk-benefit balance. In our setting, we should not perform MT in distal M2 or M2 having caliber < 2.0mm procedures due to insufficient evidence of their benefits in international and local data. Additionally, there is currently no guideline, randomized controlled trial (RCT), or meta-analysis available on this specific scenario.

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7	Tandem Occlusion, 18-50 years, LKW < 6 hours, NIHSS > 6, CT ASPECT > 6, CTA poor/ fair collaterals, CTP salvageable brain tissue.	tPA & MT with possibility of PTA/Carotid stenting.	The risk of complications increases when EVT is not pursued compared to offering the treatment. Given the age group, mechanical thrombectomy (MT) should be carried out.	In this specific situation, complications are expected to arise. The INR/neuro-interventionist, neurologist, and neurosurgeon should convene to discuss potential adverse outcomes and make preparations for managing them.
8	Isolated proximal Extracranial ICA occlusion, 18-80 years, LKW 4.5 -24 hours, CT ASPECT ≥5	Best Medical Management	The risk-to-benefit ratio is nearly equal between best medical management (BMM) and endovascular therapy (EVT). There is no documented advantage of EVT in this clinical scenario.	There is no available international or local data supporting the beneficial role of endovascular therapy (EVT) in isolated extra-cranial proximal internal carotid artery (ICA) occlusion. Clinical outcomes between best medical management (BMM) and EVT are comparable. Given the financial constraints, logistical challenges, and available medical resources, there is no apparent advantage in pursuing EVT for proximal isolated ICA occlusion. Moreover, the added risks associated with percutaneous transluminal angioplasty (PTA) and emergency stenting may further compromise clinical outcomes.
9	Isolated Intracranial ICA Occlusion (High), Age < 60,< 6 hours, CT ASPECT ≥ 5, NIHSS > 6 or NIHSS < 6 with disabling stroke, Non-opacification of ACA/MCA or both	tPA(If in window) & MT	The risk-to-benefit ratio is slightly better than best medical management (BMM) and endovascular therapy (EVT). (21)	
10	Posterior circulation stroke, 18-80 years, NIHSS>10, LKW<12 hours, pcASPECT CT> 6,CTA posterior circulation occlusion	tPA if in window & MT	Proceed with EVT if the eligibility criteria of ATTENTION trial is met.	Strict adherence to eligibility criteria is necessary because poor clinical outcomes are anticipated in posterior circulation stroke cases.
11	Posterior circulation stroke, 18-80 years, NIHSS>6, LKW < 4.5 hours, pcASPECT CT> 6,CTA posterior circulation occlusion	tPA & MT	Proceed with EVT even tPA is still running.	Strict adherence to eligibility criteria is necessary because poor clinical outcomes are anticipated in posterior circulation stroke cases.
12	Posterior circulation stroke, 18-80 years, NIHSS>6 or NIHSS < 6 with disabling stroke, LKW 6- 24 hours, pcASPECT CT> 6,CTA posterior circulation occlusion, MRI Brain viable brain stem	MT	Proceed with EVT.	Strict adherence to eligibility criteria is necessary because poor clinical outcomes are anticipated in posterior circulation stroke cases.

LVO = Large vessel occlusion, MVO = medium vessel occlusion, RCT = Randomized control trials, mRS = Modified Rankin Scale, LKW = Last known well, NIHSS=National Institute of Health Stroke Scale, AIS = Acute ischemic stroke, MCA = middle cerebral artery, ICA = Internal carotid artery, EVT = Endovascular therapy,tPA = tissue plasminogen activator, MT = Mechanical thrombectomy, MRI = Magnetic resonance imaging, ACA = Anterior cerebral artery, PTA = percutaneous transluminal angioplasty,BMM = best medical management, INR = international normalized ratio, pcASPECT = posterior circulation Alberta Stroke Early Computed Tomography, CTA = Computed tomography angiography, CTP= Computed tomography perfusion,, DWI=Diffusion weighted imaging, FLAIR=Fluid attenuated inversion recovery, T2WI = T2 weighted Imaging, ICA = Internal carotid artery

Tomography Score
BA = Basilar artery
BMM = Best medical management
CT = computed tomography
CTA = computed tomographic angiography
CTP = computed tomography perfusion
EVT = Endo-vascular management
ICA = Internal carotid artery

LKW = Last known well.
LVO = large vessel occlusion
MCA = Middle cerebral artery
MT = Mechanical thrombectomy
mRS = modified Rankin scale
MVO = medium vessel occlusion
NIHSS = National Institutes of Health Stroke Scale
PICO = Population, Intervention, Comparisons and Outcome
PTA = Percutaneous transluminal angioplasty
RCT = Randomized clinical trial
tPA = Tissue plasminogen activator
VA = Vertebral artery

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