

Optimal Use of Temporary Clip Application during Aneurysm Surgery – In Search of the Holy Grail

Abstract

Temporary clips are invaluable safety tools during the clipping of an aneurysm. Controversies regarding maximum permissible duration and safety, however, remain unanswered. This descriptive narrative attempts to review the literature to provide valuable insights on controversies clouding the use of temporary clips among neurosurgeons. Popular databases, including Pub Med, Medline/ Medscape, Scopus, Cochrane, Embase, Google Scholar, were searched to find available literature on temporary clips. The searched MeSH terms were “Temporary Clip,” “Temporary Clipping,” “Cerebral Aneurysm,” and “Aneurysm.” Temporary clips have been in use since 1928 and have undergone considerable structural and technical modifications. A temporary clip’s optimal safety limit is not yet defined with literature evidence ranging from immediate to 93 min. It is not yet definite whether temporary clips application aggravates vasospasm, but emergency temporary clips application, especially in poor-grade aneurysmal subarachnoid hemorrhage patients, is associated with poor outcomes. A temporary clip needs to be applied with caution in patients treated earlier by endovascular technique and having indwelling stents. Nitinol Stent is feasible, while a Cobalt-Chromium alloy stent does not get occluded and gets deformed under the closing pressure of a temporary clip. Although a temporary clip application is a fundamental strategy during the clipping of an aneurysm; the exact safe duration remains to be decided in randomized control trials. Their utility for the shorter duration is beneficial under un-conclusive evidence of neuroprotective agents and intraoperative monitoring. Neurosurgeons need to consider all aspects of their pros and cons for optimal use.

Keywords: *Aneurysm, temporary clip, temporary clipping*

Introduction

The debate between clipping and coiling is far from over, and the feud seems to be evenly poised. Like interventional counterparts, vascular surgeons have been continually trying to optimize their surgical strategies to improve outcomes. The uncertainty over the use of temporary clips continues to plague them. A temporary clip is like a double-edged sword— both lifesaving as well as life-threatening. While a planned elective temporary clip application may ensure perfect obliteration of an aneurysm, an emergency temporary clip applied inappropriately may produce catastrophic consequences. Questions regarding the optimal duration of the temporary clip, single vs. intermittent use, use of intraoperative monitoring, and whether conditioning is beneficial to remain unanswered. Even with a better

understanding of the disease, improved neuro-anesthesia techniques, and brain protection strategies, vascular surgeons are hesitant to use temporary clips. This review intends to address those troublesome dubieties and pave the way for smooth clipping for neurosurgeons.

Evolution of Temporary Clips and their Biomechanics

Temporary clips differ from permanent clips in having lesser closing pressures compared to the permanent ones. They also are less traumatic to the vessel and its endothelium. Since their first use by Dr. Jefferson in 1928,^[1] temporary clips have undergone various modifications in shape, metal properties, and closing pressures. These facelifts have turned them into useful safety tools in the armamentarium of neurovascular surgeons. The most commonly used Yasargil’s temporary

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Access this article online

Website: www.asianjns.org

DOI: 10.4103/ajns.AJNS_465_20

Quick Response Code:



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How to cite this article: Kumar S, Sahana D, Menon G. Optimal use of temporary clip application during aneurysm surgery – In search of the holy grail. *Asian J Neurosurg* 2021;16:237-42.

Submitted: 11-Oct-2020

Accepted: 29-Jan-2021

Published: 28-May-2021

clips have closing pressures in the range of 0.88–1.08 N, nearly 60% of their permanent counterparts.^[2] The closing pressure is least at the tip, and therefore when used, they should be placed perpendicular to the vessel engaging the tip maximally. Experimental studies on rats have shown a role of endothelial-derived growth factor in relaxing the vasculature after a temporary clip application. There is a decrease in endothelium-derived relaxing factor levels after longer durations (>10 min) of temporary clipping suggesting their role in thrombus formation leading to vessel occlusions.^[3] When multiple applications are needed, endothelial damage may be minimized by intermittent application over different vessel segments.

Indications for Temporary Clip Application

Temporary clips are an aid during aneurysm surgery. They are applied to the vessels proximal to the aneurysm to assist in aneurysm dissection. It is a rule rather than an exception to prepare a sufficient length of the proximal vessel free from perforators, before dissection of the aneurysm. Temporary clips are applied either as a planned elective step or as an emergency rescue measure. An elective temporary clip application may be made for various indications. They help to reduce the aneurysm turgor before clip application. They also assist in delineating the aneurysm morphology better, especially while dissecting complex aneurysms. They are also useful electively during suction decompression technique, remodeling of the sac, and removal of atherosclerotic plaque from the neck, precluding occlusion during permanent clipping. Emergency temporary clip applications are required during intraoperative rupture to control bleeding and facilitate further dissection and permanent clipping.

Risks of Temporary Clip Application

A temporary clip application is not devoid of its ill-effects. Although they are designed to limit damage to parent vessels, prolonged applications may result in ischemia, adding to surgical morbidity. Search for the ideal time limit permissible for safe application of temporary clip remains an elusive Holy Grail for vascular surgeons.

Assessments of ischemic events after temporary occlusions are evaluated using intraoperative electrophysiological, clinical, and radiological methods. Intraoperative monitoring is done using motor evoked potentials (MEPs) and somatosensory evoked potentials (SSEP). Delayed ischemic neurological deficits (DIND) refers to new-onset neurological deficits in subarachnoid hemorrhage (SAH) patients in whom other causes have been ruled out. Similarly, new-onset computed tomography (CT) demonstrable ischemic areas after SAH that develop within 4–14 days and are not explainable by other causes were labeled as delayed cerebral infarction (DCI).^[4] CT scan has been the most widely used radiological modality for establishing DIND and DCI. Diffusion-weighted magnetic

resonance imaging can diagnose even silent ischemic events in the order of 9.8% per treated aneurysm, according to Krayenbuhl *et al.*, who reported one symptomatic and five silent ischemic lesions out of 51 aneurysm patients.^[5]

Safety Duration of Temporary Clip

The maximal permissible time limit for a temporary clip's safe application remains the most controversial issue to address. The maximum safe occlusion time reported in the literature is by McDermott *et al.*, who, in 1989, reported a good recovery in a giant middle cerebral artery (MCA) aneurysm after 93 min of temporary clip application under barbiturate protection.^[6]

The window period for chemical and mechanical thrombectomy has been progressively increasing. The DAWN trial concluded that improved outcomes after thrombectomy for ischaemic strokes might be achieved within 6–24 h of the time last known well, and several authors claim to have pushed it even beyond 24 h.^[7,8] It can therefore be argued that temporary clips applied under brain protection for a few minutes, ideally, should not be causing ischemic deficits.

In the long-term follow-up study of 382 patients with SAH and 246 patients of unruptured aneurysms, temporary clipping did not affect the long term outcomes. The mean duration of total temporary artery occlusion was 19.4 min in the SAH group and 16.1 min in the unruptured group.^[9,10] The same duration (20 min) has been found in another study.^[11]

Silva *et al.* demonstrated variations in the fall of regional brain tissue oxygenation (PbtO₂) following temporary clipping, depending upon the brain regions, with temporal lobes (MCA and PCom aneurysms) showing higher falls compared to the frontal.^[12] The safety limit of temporary clipping time should ideally be studied on vessels with the least chances of having collateral circulation, like the M1 segment of MCA. The first attempt with this idea was made in the late 90s by Lavine *et al.* when a safe temporary clipping time up to 10 min was demonstrated under intravenous brain protection (thiopental, propofol, and etomidate). All patients who underwent temporary clip application for 10 min or more, without brain-protective agents developed infarction, whereas only five of 23 patients developed infarction when brain protection was used.^[13] Kameda *et al.*, in his study in 2020, reported maximal safe clipping time as 5 min under electrophysiological monitoring,^[14] which was considerably higher than that reported by Tanabe *et al.* in 2017 (2.4 min).^[15]

With the improvement in technology, it is possible to detect ischemic changes faster at cellular levels even before their clinical manifestations, thereby improving clip application safety. These have led to a reduction in the permissible occlusion time, from 93 min to 2.4 min.

Factors Influencing the Safety Limits of Temporary Clip Application

Delayed neurological deficits secondary to vasospasm remain a dreaded complication following aneurysmal SAH. The prolonged application of temporary clips can result in ischemic complications independent of vasospasm. It is difficult to differentiate whether ischemic deficits following aneurysm surgery are related to temporary clip application or due to vasospasm. Deficits occurring soon after surgery, in an otherwise intact patient, should be attributed to temporary clip application provided accuracy of clip placement has been confirmed by angiography. Malinova *et al.* studied 778 patients undergoing aneurysm clipping, where temporary clips were applied in 338 (43.4%) patients. The study group included all grades of SAH. They did not observe overall increased incidences of TCD vasospasm, DIND, or DCI associated with temporary clipping. On multivariate analysis, however, DCI and DIND were significantly higher in patients with higher Fisher grades. Poor WFNS Grade (Grade IV-V) patients had a higher chance of DCI with an increasing trend toward DIND, though not reaching statistical significance.^[4] Silva *et al.*, in their study of 41 patients, reported DCI in six (14.6%) patients, five of which were with poor Hunt and Hess grade (Grade III and IV), one with grade II and none in Grade I or un-ruptured group.^[12] In a study that included predominantly poor grade patients, Woertgen *et al.* observed that a longer duration of temporary clipping (10 or more minutes) was associated with vasospasm at a mean interval of 6.4 days after ictus.^[16]

Therefore, it may be concluded that patients with poor-grade SAH have a higher risk of vasospasm related deficits and temporary clip application in such patients probably accelerates the ischemic process. Rescue temporary clipping is a predictor of higher DCIs in comparison to elective temporary clipping, which, on the contrary, has not been found associated with TCD vasospasm, DIND, and DCI.^[4]

How to Improve the Safety Limit?

Use of neurophysiological monitoring

Concomitant use of neurophysiological monitoring further enhances the safety of temporary clip application. Electrophysiological monitoring (MEP, and SSEP) and intraoperative thermal diffusion flowmetry have been tried by different authors to predict the onset of ischemic events during temporary clip application.

MEP can be monitored in two ways, direct cortical MEP and trans-cranial MEP. Combined use of both has been shown to improve reliability and permit a longer duration of temporary occlusion.^[17] In a study by Kameda *et al.*, episodes of temporary clippings in nine MCA aneurysms were monitored using MEP via direct cortical

stimulation.^[14] Temporary clips were released when there was a reduction in MEP amplitude of more than 50%. After logistic regression analysis, the safe single continuous application time recommended by the authors was 312 s (Nearly 5 min), much less than the earlier recommendations by Lavine *et al.*^[13] Kameda *et al.* further observed that the total time was not significantly higher for multiple intermittent temporary clip applications. In their series, two patients developed transient deficits that recovered in the postoperative period.^[14] The safe time limit under MEP monitoring reported by Tanabe *et al.* was up to 2.4 min, considerably shorter than the previous authors.^[15] In another retrospective review by the Pittsburgh group, overall, 6% of patients developed peri-operative stroke (<24 h), and the maximum mean duration, after single temporary occlusion, was 12.6 min for patients who developed peri-operative stroke and 8 min in those who did not.^[18]

SSEP is another intraoperative monitoring modality where a decrease in amplitude by >50% or an increase in latency by >10% is a predictor for adverse neurological events. It has a sensitivity of 25%–50%, a specificity of 84%–95%, a positive predictive value of 16%–30%, and a negative predictive value of 94%–97% for postoperative strokes.^[18,19]

Electrophysiological monitoring predictions are not always accurate, and ischemic deficits can develop even in the absence of MEP and SSEP changes. In their study on thirty cases of un-ruptured aneurysms under electrophysiological monitoring, Abdulrauf *et al.* observed immediate neurological deficit in three cases, without synchronous MEP, SSEP, or electroencephalography (EEG) changes.^[20] Similar discrepancies were reported by Suzuki *et al.* in 2 of 5 cases of ICA aneurysms.^[21]

A review of these studies fails to clear the clouds of mystery around the maximum safe duration of temporary clipping. Electrophysiological monitoring looks promising but is far from being absolute. One cannot be sure that a patient with transient drops in MEP or SSEP will have neurological deficits after recovery from anesthesia. Motivated by these observations, the authors are conducting a study (unpublished) using intraoperative electrophysiological monitoring during temporary clipping. The preliminary results of trans-cranial MEP monitoring on three MCA aneurysms showed safe clipping durations as 293, 327, and 374 s (Mean 331 s) under intra-venous propofol neuro-protection. Additional cases should provide better insight into this issue.

The events after temporary occlusions are limited not only to motor impairments but cognitive dysfunctions as well. Long-term cognitive disturbances may persist even without motor deficits or radiological infarcts. In a prospective trial on Anterior communicating artery aneurysms patients with good Hunt and Hess grades, the mean duration of temporary occlusion was 8.2 min. There were no clinical

or radiological strokes, but patients without temporary clip applications had better cognitive functions.^[22] Under ischemic stress during temporary clipping, the neurons of the vascular territory survive on collateral circulation and vasodilatory response to acute ischemia. This concept was validated by measuring regional cortical blood flow using a thermal diffusion flow probe study before and after temporary clipping. In a study by Ohmoto *et al.* in 1991, a safe occlusion time of 15 min was reported, before cortical blood flow decreased below the critical levels of 30 ml/100 g/min.^[23] The reduction of cortical blood flow was less apparent with ICA occlusion than the M1 segment of MCA occlusion, possibly because of collateral circulation across ACom.

These findings strengthen the belief that tolerance limits of ischemia vary from the brain to brain, and all temporary clips should be applied under some form of monitoring.

Intermittent multiple clip application

Intermittent clipping is believed to be better and safer than single continuous clipping over a more extended period. The time between subsequent clip applications and reperfusion time has not been described consistently. Most authors wait until the return of intraoperative monitoring parameters to baseline before reapplication. Kashkoush *et al.* described a median time of 3.3 min for the return of SSEP findings to baseline following temporary clip readjustment.^[18]

Preconditioning and postconditioning

Conditioning the brain before temporary vessel occlusion provides an extra margin of safety for tolerance to ischemia. Since its inception, neuroscientists have been on the lookout to improve these preconditioning strategies, using induced hypothermia, adenosine-induced circulation arrest, raising the mean blood pressure, burst suppression with barbiturates, and use of etomidate and propofol. Their effects have been studied using intraoperative monitoring with PbtO₂, MEP, SSEP, and EEG and clinical outcome parameters. Barbiturates have long been used for burst suppression, monitored by BIS and EEG. Their use with propofol provides more prolonged suppression and better neuroprotection than with sevoflurane-nitrous anesthesia.^[24] There exists dissensus in the literature regarding the use of propofol. In one clinical trial, propofol infusion at 1.2 µg/ml post temporary clipping reduced oxidative stress and improved cognition,^[25] while another clinical trial failed to show any benefit of propofol on cognition.^[26] Intra-operative hypothermia for aneurysm surgery trial, a multicentre randomized control trial, concluded that short term (24 h) and long term (3 months) neurological outcomes are not better with mild hypothermia (33°C) and with the use of barbiturates.^[27] There has not been any consensus regarding practice guidelines, optimal dosage, duration, and actual benefits using neuroprotective agents, and institutional protocols vary.

The effectiveness of postconditioning in nonneurological tissues such as cardiac, renal, and muscles are well established. Several experimental animal studies successfully reflected these observations on neuronal cells as well.^[28,29] Global luxury perfusion due to dysautoregulation is well established after SAH.^[30,31] In a Xenon CT perfusion-based study by Araki *et al.*, significantly higher incidences of hyper-perfusion along with related cerebral infarcts were observed after microsurgical clipping of ruptured aneurysms. Focal hyper-perfusion was observed in eight of the 16 patients with temporary clipping but not in five patients without temporary clipping. They also reported a longer total mean temporary clip time (31.9 vs. 13.9 min) and mean maximum single temporary clip time (18.4 vs. 8.6 min) in those with hyper-perfusion compared to those without it. The events of hyper-perfusion were markedly increased after >20 min of occlusion time.^[32] In unruptured aneurysms, similar observations were seen on SPECT after temporary occlusions by Iwata *et al.* (3 min) and Kuroki *et al.* (7 min).^[30,31]

The above studies suggest that temporary clipping aggravates reperfusion injuries. Postconditioning may reduce these injuries. Releasing the temporary clip in a stuttered manner allows gradual reperfusion of neuronal tissue and prevents ischemic stress from hyper-perfusion injury at cellular levels.

Special situations

With the number of endovascular interventions rising each day, aneurysm surgeons now have to face a new entity-residual or recurrent aneurysm in a previously coiled or stented vessel. The presence of a stent in the vessel proximal to the aneurysm is a cause of serious concern. In an animal study, Darsaut *et al.* showed repeated clip slippages, inadequate occlusions, damage to the device, and increased risk of thrombo-embolic strokes after clip occlusion of “Pipeline flow” diverted vessels.^[33] In an *in vivo* study on synthetic vessels made of silicon, three self-expanding stents, Neuroform by Boston Scientific, Enterprise stent by Codman, and Pipeline flow diverting stent by Medtronic, were studied. After temporary clip application, Neuroform and Enterprise stents, both made of Nickel-Titanium alloy (Nitinol), showed immediate flow arrest and return to original shape on clip removal. Pipeline flow diverting stents made up of Cobalt-Chromium alloy showed flow arrest only after second clip application and were deformed irreversibly with a reduction in luminal diameter.^[34] These observations should be kept in mind, and under these circumstances, surgeons need to isolate a vessel segment distal to the device, which is often difficult.

Conclusions

The temporary clip is a handy intraoperative tool in the armamentarium of an aneurysm surgeon. However, the ideal safe duration for its application remains undetermined

and varies depending upon the modality of physiological monitoring used. Controlled trials with the integration of combined multiple monitoring modalities may provide valuable insights. Until then, surgeons should use temporary clips under appropriate circumstances and indications, keeping the occlusion time as short as possible, preferably with intraoperative monitoring and neuroprotection.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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