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Endovascular Thrombectomy for Patients Over the Age of 75 with Acute Ischemic Stroke: A Systematic Review

Kiné Ndoye

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A Major Paper Presented

by

Kiné Ndoye

Approved:

Committee Chairperson _____ _____
(Date)

Committee Members _____ _____
(Date)

_____ _____
(Date)

Director of Master's Program _____ _____
(Date)

Dean, School of Nursing _____ _____
(Date)

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Abstract

Stroke is a leading cause of disability and death worldwide. According to Slawski et al. (2018), strokes will more than double in 2050, with the greatest percentage of affected patients being over the age of 75. Administering interventions to patients affected by acute ischemic stroke (AIS) has been a controversial topic when elderly patients were involved (Alawieh et al., 2018). Elderly patients have been known to be excluded from clinical trials solely due to their age and comorbidities (Karhi et al., 2018). The purpose of this project was to determine if the use of endovascular thrombectomy (EVT) is recommended for elderly patients over the age of 75 years of age who have suffered an acute ischemic stroke from a large vessel occlusion (LVO). Six studies met inclusion and were included in this systematic review. The overall findings of this systematic review suggest the use of EVT to be effective for elderly patients over the age of 75 years of age who have suffered an AIS from an LVO. Despite high mortality rates and less favorable outcomes in the elderly cohorts in the six studies, four of the six articles concluded that the alternative of not providing thrombectomy could have detrimental outcomes. Implications of this systematic review include the importance of the advanced practice nurse's (APRN) role in advocating and educating patients and families about the benefits of receiving thrombectomy after suffering an AIS from an LVO. In addition, APRNs should educate their colleagues about the evidence regarding thrombectomy in order help bridge the gap in the lack of knowledge regarding EVT in the elderly population.

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ENDOVASCULAR THROMBECTOMY FOR PATIENTS OVER THE AGE OF 75 WITH ACUTE ISCHEMIC STROKE: A SYSTEMATIC REVIEW

Background/Statement of the Problem

Stroke is a leading cause of disability and death worldwide. According to Slawski et al. (2018), approximately 30% of strokes affect patients over the age of 80, with 17% of those patients being over the age of 85. The authors state that by 2050, strokes will more than double, with the greatest percentage of affected patients being over the age of 75. With the progression of technology, there are many interventions that have, in many opinions, either mitigated the detrimental effects of strokes or contributed to its associated mortality rate. Administering interventions to patients affected by acute ischemic stroke (AIS) has been a controversial topic when elderly patients were involved (Alawieh et al., 2018). Elderly patients have been known to be excluded from clinical trials solely due to their age and comorbidities (Karhi et al., 2018).

An ischemic stroke occurs when there is a clot in a blood vessel in the brain depriving oxygen to that area. Intravenously administered tissue plasminogen activator (tPA), also known as alteplase, is one of the most widely known interventions for AIS. This medication is a protein that lyses or breaks down blood clots to allow reperfusion to the area of the brain where the blood vessel was once occluded. Endovascular thrombectomy (EVT) has proven efficacy and safety and is considered the gold standard for treating AIS patients with large vessel occlusions (LVO) regardless of whether tPA was administered prior to EVT (Meyer et al., 2020). Evaluation for tPA administration and EVT happens simultaneously (Powers et al., 2019). Tissue plasminogen activator can

be administered prior to EVT if no contraindications to tPA exist; contraindications will be discussed below in the 'standard treatment for AIS' section.

It is crucial to determine whether lifesaving treatments prolong elderly patients' quality and/or quantity of life. Family members and or patients should carefully consider the side effects of these potentially lifesaving treatments. Preexisting conditions and baseline functionality should be taken into consideration as these are pertinent factors in the decision to accept or decline treatment. Co-morbid conditions greatly impact quality of life and should considered when determining appropriate treatment options for each patient. Stroke severity and treatment timeframe affect a patient's outcome and quality of life. It is crucial to bridge the gap in the lack of knowledge regarding outcomes of AIS treatments in the elderly population. Malhotra et al. (2019) discuss concerns raised about the use of thrombectomy in elderly patients related to poor functional outcomes. On the other hand, the American Stroke Association's (ASA) 2019 updated guidelines did not include an age cut off for EVT. The patient does, however, have to be over the age of 18, (Powers et al., 2019). Nonetheless, the guidelines advise the careful consideration of patient comorbidities when considering treatment options.

The purpose of this project was to determine if the use of endovascular thrombectomy is recommended for elderly patients over the age of 75 years of age who have suffered an acute ischemic stroke from a large vessel occlusion.

Next, a review of the literature will be presented.

Literature Review

An extensive search in the Cumulative Index of Nursing and Allied Health Literature (CINAHL) Plus with Full Text, PubMed, and Google Scholar databases was conducted to find articles published about endovascular thrombectomy in elderly patients who have suffered AIS with an LVO. Keywords searched included: endovascular thrombectomy, ischemic stroke, hemorrhagic stroke, transient ischemic stroke, tPA, stroke and age-related complications, stroke and co-morbidities, efficacy of endovascular thrombectomy, endovascular treatment, and benefits to thrombectomy for elderly patients. Articles written between 2010 and 2021 were reviewed to determine the efficacy of endovascular thrombectomy for patients who have suffered an acute ischemic stroke involving a large vessel occlusion. The administration of tPA was not a contraindication to EVT in the articles, nor was tPA an exclusion to the studies.

Stroke Pathophysiology

An ischemic stroke occurs when a clot compromises perfusion of the brain and deprives it of oxygen and nutrients and is the most common type of stroke, accounting for 83% of all strokes. Hemorrhagic stroke accounts for 17% of all strokes and is outside the scope of this review. Transient ischemic attack (TIA) is considered a ‘mini stroke’ and a warning sign of an impending stroke. TIAs occur in two percent of adults in the United States and are also outside the scope of this review (Barkley, 2021).

There are modifiable and nonmodifiable risk factors for ischemic stroke. Modifiable risk factors include hypertension, diabetes, atrial fibrillation, hypercholesteremia, hyper-coagulopathy, smoking, alcohol use, sedentary lifestyle, oral contraceptives, hormone replacement therapy, and illicit drug use. Nonmodifiable risk

factors include heart disease, prior stroke, advanced age, male gender, older female, race/ethnicity, family history of stroke, polycythemia, and sickle cell disease (Kuriakose et al., 2020). The treatment of modifiable risk factors and cessation of activities that induce a stroke can greatly reduce one's chance of developing a stroke.

Ischemic Stroke

The flow of blood to the brain is controlled by two internal carotid arteries and two vertebral arteries. A stroke occurs when blood flow to an area of the brain is disrupted thus causing oxygen deprivation to the cerebral tissue. The source of an ischemic stroke can be a thrombus or an embolus. Thrombi, the most common cause of ischemic stroke, occur in atherosclerotic blood vessels; plaque build-up and platelet aggregation cause blood clots to form in arteries that circulate blood to the brain (Kuriakose et al., 2020). Atherosclerotic plaques are most often found at arterial bifurcations like those found in the internal carotid and vertebral arteries (Norris, 2019). As previously mentioned, these arteries carry blood flow to the brain; when plaque impedes oxygen rich blood flow to the brain, a thrombotic stroke ensues (Kuriakose et al., 2020). Thrombotic strokes are most commonly seen in older adults with atherosclerotic heart or peripheral arterial disease (Norris, 2019).

Embolic ischemic stroke occurs when a blood clot originates elsewhere and travels to the brain. According to Gire & Wice (2017, p. 292), an embolus can also result from fragments of atheromatous plaques, lipids, or air. The embolus embeds itself in a smaller artery and obstructs blood flow to an area in the brain causing cell death. According to Norris (2019), embolic strokes most often occur in the middle cerebral artery from thrombi in the left side of the heart or from atherosclerotic plaque in the

carotid arteries which dislodge and travel, eventually blocking the vessel. Embolic strokes may be of cardiac origin, secondary to a myocardial infarction or atrial fibrillation (Gire & Wice, 2017, p. 292). Other cardiac conditions such as rheumatic heart disease, ventricular aneurysm, and bacterial endocarditis may also contribute to the formation of emboli (Norris, 2019).

Ischemic strokes can occur without a known source of origin (cryptogenic). According to Kamtchum-Tatuene et al. (2021), ischemic stroke is considered cryptogenic when specific etiology is unknown; cryptogenic strokes represent approximately 30% of all ischemic strokes. There are three subgroups of cryptogenic strokes: stroke with no cause despite complete workup, stroke with various possible underlying causes, and stroke with incomplete baseline workup. Stroke with no cause despite complete workup is defined as an embolic stroke of unknown source (ESUS) (Kamtchum-Tatuene et al., 2021). The etiology of ESUS is presumed embolic despite the absence of an identifiable cardiac or arterial embolic source (Kamtchum-Tatuene et al., 2021). Embolic stroke of unknown source refers specifically to non-lacunar stroke; it represents one of five types of ischemic strokes (Kamtchum-Tatuene et al., 2021). Lacunar infarct is defined by Micheli & Corea (2012), as small deep infarcts (less than 15 mm in diameter) in a single penetrating artery.

Ischemic Stroke Patients Ineligible for Thrombolytics or EVT

Recommended interventions may not be appropriate for all AIS patients as individuals may have a blocked cerebral vessel that is too distal to retrieve via thrombectomy or the patient may be outside the EVT and/or treatment windows. Also, patients may receive interventions without successful recanalization/perfusion. In these

cases, hypertension will be allowed in the first 24 hours to allow as much perfusion to the brain as possible. The patient will be monitored in the hospital and immediately placed on antiplatelet therapy (Powers et al., 2019). To prevent future ischemic stroke, the American Stroke Association [ASA], (n.d.) recommends aspirin 50-325 mg daily or clopidogrel 75 mg daily; in some instances, dual therapy is recommended short term or for specific patient cases.

Standard Treatment for Ischemic Stroke

Early recognition of stroke symptoms and advancement in treatment options have contributed to stroke declining from the fourth leading cause of death in 2008 to the fifth leading cause of death in 2013, according to Yang et al. (2017). In the United States, stroke is still the fifth leading cause of death, behind heart disease, cancer, chronic lower respiratory disease, and unintentional injuries/accidents. Worldwide, stroke is the second leading cause of death after heart disease. Stroke continues to be a leading cause of serious long-term disability, with an annual cost of approximately $33.9 billion (Yang et al., 2017). Currently approved treatments for ischemic stroke include intravenous thrombolytics, e.g., tPA, and/or performing endovascular procedures, e.g., EVT. However, these interventions may not be indicated for all patients (Powers et al., 2019).

Thrombolytics

Tissue plasminogen activator (also known as alteplase) was approved for the treatment acute ischemic stroke by the U.S. Food and Drug Administration (FDA) in 1996 (Tu, 2015). Tissue plasminogen activator, the gold standard and FDA approved thrombolytic agent for acute stroke, is a protein that breaks down blood clots to restore blood flow to a previously occluded area in the brain (Ischemic Stroke Treatment, 2018).

According to the updated 2019 ASA guidelines, tPA should only be administered within 4.5 hours after the onset of stroke symptoms. Prior to administration, a computerized tomography (CT) scan of the brain must be completed to rule out a hemorrhagic stroke and blood pressures must be below 185/110 mm Hg prior to administration. Additionally, there here must be no recent trauma or surgery and no intake of anticoagulant medication in the last 24 hours. During the administration of tPA and the next 24 hours that ensue, close monitoring of patients is pivotal because intracerebral hemorrhage (ICH) is a fatal side effect of tPA.

Tenecteplase and reteplase are two thrombolytics still under research for the use of acute ischemic stroke. Currently, these two thrombolytics are only indicated for the management of acute myocardial infarction and have not been FDA approved for acute ischemic stroke (Zitek et al., 2020). However, the updated 2019 ASA guidelines, recognize that some institutions are moving towards the use of tenecteplase as first line treatment of AIS in lieu of alteplase. According to Zitek et al. (2020) tenecteplase should be the preferred treatment of AIS over alteplase as tenecteplase has greater fibrin specificity, a longer half-life than alteplase, is less expensive, easier to administer, and may cause less bleeding complications than alteplase. Despite these reasons, Zitek et al. report the FDA has yet to approve tenecteplase for AIS in the United States although its use is becoming more common.

Endovascular Thrombectomy (EVT)

Endovascular thrombectomy has become the gold standard for treating patients with a large vessel occlusive stroke who are eligible according to criteria (Powers et al., 2019). Large vessel occlusions (LVO) can occur in the anterior circulation which consists

of the internal carotid (ICA), middle cerebral (MCA), and anterior cerebral (ACA) arteries. They can also occur in the posterior circulation which includes the posterior cerebral (PCA), vertebral, and basilar arteries. (Gire & Wice, 2017, p. 291). If diagnostic imaging confirms the presence of an LVO, thrombectomy can be performed up to 24 hours after the onset of symptoms, per the updated 2019 ASA guidelines. Thrombectomy is an endovascular procedure that involves the use of a wire-cage device called a stent retriever; a catheter is threaded through the right femoral artery or the right radial artery to retrieve the clot in the brain (Powers et al., 2019). Over the next 24 hours, it is vital to monitor the groin or radial puncture site closely for hemorrhage and the presence of pulses.

The updated 2019 ASA guidelines recommend treating eligible acute ischemic stroke patients with large vessel occlusion with intravenous thrombolysis in addition to endovascular thrombectomy. Mistry et al. (2017) emphasize the pros and cons to receiving a dual therapy for ASI. For example, pre-treatment with intravenous thrombolysis may extend the time it takes to receive thrombectomy, especially in smaller hospitals that use the drip and ship method of care. The smaller hospitals may only be able to administer tPA and then transfer patients to alternative locations to undergo EVT. Alternatively, administration of intravenous thrombolytics such as tPA can lyse the clot thus negating the need for thrombectomy; tPA is also beneficial for clots that are too distal for successful endovascular retrieval. There is a risk of hemorrhagic transformation, previously referred to as hemorrhagic conversion, with the administration of intravenous thrombolytics. This risk was discussed by Mistry et al.; however, their results showed equal odds of transformational hemorrhage in patients who received tPA

with EVT and those who underwent EVT without prior administration of tPA. According to the researchers, EVT attains a 70% to 80% success rate in patients with an LVO, while intravenous thrombolysis without EVT has a 6% to 30% success rate in patients with an LVO. A study by Karhi et al. (2018), supports the use of tPA and EVT together as their combined use provides significantly greater outcome as compared to using tPA alone for AIS patients with an LVO.

Stroke in Elderly Patients

The updated 2019 ASA guidelines for treating patients who have suffered an AIS from an LVO do not exclude patients over the age of 75 from EVT procedures (Powers et al., 2019). A research article by Malhotra et al. (2019) showed that EVT in elderly patients (over 80 years old) revealed more favorable outcomes than tPA treatment alone. Although Malhotra et al., discuss concerns raised about the use of EVT in elderly patients related to poor functional outcomes, the ASA guidelines have no adult age restrictions for EVT (Powers et al., 2019). Nonetheless, when considering treatment options, the guidelines advise the careful consideration of preexisting conditions in addition to the patient's quality and quantity of life (Powers et al., 2019). Thus, the purpose of this project was to determine if the use of endovascular thrombectomy (EVT) is recommended for elderly patients over the age of 75 years of age who have suffered an acute ischemic stroke from a large vessel.

Age-related complications.

The incidence of stroke increases with age and the risk doubles after the age of 55 (Kuriakose et al., 2020). Men under the age of 44 are hospitalized for AIS at a higher rate than women in the same age group and one in five women between the ages of 55 and 75

in the United States are at risk for a stroke (CDC, n.d.-b). Men have a higher incidence of stroke but as women age, their stroke incidences rise as a result of their longer life expectancy; women die more from strokes because they are living longer (Norris, 2019). Women over the age of 75 with atrial fibrillation have a 20% increased risk of a stroke, thus cardioembolic stroke occurs more often in women (Kuriakose et al., 2020). As previously mentioned, ASA guidelines do not recommend an age cut off for EVT, but patient comorbidities and baseline functional status should be taken into consideration (Powers et al., 2019).

Theoretical Framework

Evidence-based practice (EBP) allows healthcare professionals to rely on research findings and science rather than tradition and belief. Evidence-based practice involves recognizing a clinical issue, examining the literature, critically appraising the literature, and establishing suitable interventions. Theoretical models of EBP guide advanced practice professionals to endorse EBP, cultivate practice standards, protocols, and interventions (McEwen et al., 2014).

The Iowa Model of Evidence-Based Practice to Promote Quality Care (see Appendix A) was the theoretical framework used to guide this project. This model guides nurses and advanced practice professionals when making clinical decisions that affect patients (McEwen et al., 2014).

According to Titler et al. (2001), the first step in the Iowa Model is to recognize either a problem-focused trigger or a knowledge-focused trigger where an EBP may need to be incorporated for change to occur. The next step is for the nurse or team to decide how much of a priority the problem is for the organization, department, or unit in which they work. Once deemed a priority, a team is created to develop, evaluate, and implement the EBP change. The team collects, analyzes, and critiques the research pertinent to the problem requiring change. The team determines whether the studies are scientifically sound and reliable enough to validate a practice change. The last step is to pilot the practice change; if successful, the organization adopts this new practice.

When the Iowa Model is applied, it aids in the delivery of quality care to patients. It is precise and has been utilized to address numerous clinical matters (McEwen et al., 2014). The foundation of this project is evidence-based research thus the best evidence is

comprehensively analyzed to provide quality care to patients. The Iowa model was utilized in this project to determine if the use of endovascular thrombectomy is recommended for elderly patients over the age of 75 years of age who have suffered an acute ischemic stroke from a large vessel occlusion.

Methods

Purpose

The purpose of this project was to determine if the use of endovascular thrombectomy is recommended for elderly patients over the age of 75 years of age who have suffered an acute ischemic stroke from a large vessel occlusion.

Inclusion/Exclusion Criteria

The inclusion criteria for this systematic review were randomized control trials (RCT) articles including subjects over the age of 75, AIS from an LVO, received thrombectomy, received tPA, and stroke occurring within 24 hours. The exclusion criteria were articles including subjects under 18 years old, patients who received tenecteplase, subjects with AIS but no LVO, studies that were not RCTs, and strokes occurring over 24 hours in the past.

Search Strategy

An extensive search in the Cumulative Index of Nursing and Allied Health Literature (CINAHL) Plus with Full Text, PubMed, and Google Scholar database was conducted to find articles published about EVT in elderly patients who suffered AIS from an LVO. This search was limited to articles published between 2015 and 2020 using the following search terms: stroke and thrombectomy in elderly patients, outcomes of endovascular thrombectomy in elderly patients, endovascular treatment and elderly patients, and benefits to thrombectomy for elderly patients.

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) framework was used in this project. PRISMA helps authors enhance the reporting of systematic reviews and meta-analyses (Moher et al., 2009). Although

randomized trials are the main focus of PRISMA, it can also be utilized in other types of research, specifically the evaluation of interventions. PRISMA is composed of a 27-item checklist (see Appendix B) that should be included when reporting a systematic review or meta-analysis along with a four-phase flow diagram (see Appendix C) which includes the different phases of a systematic review (Moher et al., 2009). The use of PRISMA is helpful when critically appraising systematic reviews but the 27-item checklist is not standard when assessing the quality of reviews.

Data Collection

Data was collected from each of the RCTs meeting criteria and recorded in tables which include: the author, year, study purpose, method, number of subjects, outcomes, results, and limitations (see Appendix D).

Critical Appraisal

The Critical Appraisal Skills Programme (CASP) was utilized to evaluate the quality of research studies. The CASP tool facilitates the critical appraisal and comprehension of research evidence, allowing the clinician to apply that evidence in practice (Oxford Centre for Triple Value Healthcare Ltd (n.d.). The tool has seven checklists (10-12 questions) divided into three sections to assess the validity of results and its relevance to practice (see Appendix E).

Cross study analysis was conducted utilizing a comparison table including each study type, adverse events, results, and limitations was created (see Appendix F).

Results

Sixty studies were identified through the initial database search with no additional studies identified through other sources. Five duplicate records were removed, and the remaining studies were screened for eligibility. Forty-nine studies were excluded during the screening process based on the inclusion and exclusion criteria of this systematic review. Six studies met inclusion and were included in this systematic review.

Clinical characteristics of the studies include EVT, alteplase, use of the baseline and postoperative National Institute of Health Stroke Scale (NIHSS), thrombolysis in cerebral infarction scores (TICI), and modified Rankin Scale (mRS). The NIHSS is a 15-item assessment tool used to measure stroke-related neurologic deficit (*NIHSS*, 2021). The TICI scores are used to grade recanalization success after EVT. A score of 0/1 means no/minimal reperfusion, 2a means partial filling of < 50% of the stroke territory, 2b means partial filling ≥ 50% of the stroke territory, 2c means near complete perfusion except for slow flow or few distal cortical emboli, and 3 is complete perfusion. Better outcomes are seen with TICI scores of 2b/2c/3 (Tung et al., 2017). The mRS is used to assess disability in patients with acute stroke; it ranges from 0, meaning no symptoms to 6, meaning death (Zeltzer, 2008).

Individual Studies

Alawieh et al. (2018) performed a multicenter retrospective chart review to evaluate thrombectomy outcomes in acute ischemic stroke due to large vessel occlusion for patients over and under the age of 80 (see Table D-1). Data was collected from seven US-based comprehensive stroke centers from 2013 to 2017. Of the 1,442 patients enrolled, 96 were excluded due to missing demographic information or procedural data.

The inclusion criteria included: patients over 18 years old with anterior or posterior circulation stroke, NIHSS score at presentation, and patients treated with stent retriever or aspiration thrombectomy as first approach. The study proceeded with the remaining 1,346 patients; 52% were women. In addition to EVT, alteplase was administered to 45.5% of the patients. Patients were separated into two cohorts < 80 years old and those aged ≥ 80 years old. There were 346 patients in the ≥ 80 group with an average age of 85 ± 5 years compared with 62 ± 13 years in the younger group. Univariate analysis showed a significantly higher percentage of women in the ≥ 80 age group (66% vs. 47%). Patients ≥ 80 years old had a considerably higher number of comorbidities than the younger cohort, i.e., hypertension and atrial fibrillation. On admission, the NIHSS score was found to be higher in the ≥ 80 age group when compared with the younger cohort (17 ± 7 vs. 16 ± 7). However, there were no significant differences found in prior stroke history, rates of posterior circulation strokes, or in tPA administration between the two groups.

The mRS at 90 days was used as the principal clinical outcome. The scores were divided into good outcome (mRS 0-2) and poor outcome (mRS 3-6). Univariate and multivariate analyses were performed to assess the independent effect of age greater than 80 years on outcome predictor. Subgroup analyses were also performed based on stroke location, recanalization success, or thrombectomy technique used. Direct aspiration first pass technique (ADAPT) was used in 58% of patients; the remaining patients underwent stent retriever thrombectomy as first-line therapy. Post-procedural reperfusion with TICI ≥ 2b was seen in 89% of cases, a good outcome was seen in 37.5% of the cases at 90 days, and the total mortality at 90 days was 24.4%. The rate of postprocedural

hemorrhage (PH) was 31%, and the rate of PH2-type hemorrhage (≥ 30% of infarcted tissue occupied by hematoma) was 4.4%. The rate of functional independence (mRS 0-2) after thrombectomy in elderly patients was considerably lower than in the younger cohort. Age ≥ 80 was independently associated with increased mortality and poor outcome at 90 days was significantly higher in the elderly population than in younger adults (35% vs 20%, respectively). Age ≥ 80 independently predicted a higher rate of postprocedural hemorrhage as compared to younger adults (42% vs 28%, respectively). This study by Alawieh et al. suggests that age ≥ 80 is associated with increased mortality and poor outcomes after EVT in multiple institutions. The study found age greater than 80 to be a predictor of poor outcomes (mRS 3–6).

A single center retrospective study by Karhi et al. (2018) was conducted at the Kuopio University Hospital in Finland between 2009 and 2015 to determine if thrombectomy in acute ischemic stroke is beneficial in octogenarians in comparison to younger patients (see Table D-2). Initially, there were 261 patients chosen, but 62 were excluded for not meeting inclusion criteria. The inclusion criteria were (a) age 18 years or older, (b) large anterior occlusion (LAO) in the M1 or M2 segment of the middle cerebral artery (MCA), or the internal carotid artery (ICA), (c) with or without an intracranial thrombus component, (d) confirmed on the admission imaging, and (e) available follow-up information for 1 year after the AIS onset. The study continued with the final 199 patients, which included 76 females. There were 162 patients under 8o years old and 37 patients over 80 years old and over. There was a higher number of females in the elderly group as compared to the younger group (78% vs. 29%, respectively). Alteplase was administered to 57% of the patients.

The study showed older patients as compared to younger patients had more complications during hospitalization (41% vs. 24%, respectively), higher 3-month mRS values (4.0 ± 2.3 vs. 2.8 ± 1.9, respectively), fewer favorable mRS values (mRS ≤ 2: 27% vs. 52%, respectively), and higher 3-month (46% vs. 10%, respectively) and 1-year mortality (49% vs. 11%, respectively). When comparing the mRS for pre-stroke and at 3 months post AIS, the older group had greater deterioration than the younger group. Although the results of the study showed a worse recovery rate in patients over the age of 80 when compared to younger patients, 27% (n = 10) of the elderly patients benefited from thrombectomy. Despite a small subject number in the elderly cohort, Karhi et al. recommended EVT for patients over 80 years old after prudent consideration.

A single center retrospective study by Kim et al. (2017) was completed at a Korean hospital between 2010 and 2015 (see Table D-3) which included 171 patients who underwent thrombectomy following AIS. Among these patients, 113 of them were over the age of 60 and were selected for the study. Patients < 60 years old with an LVO were excluded from this study. The subjects were divided in to two subgroups: the very elderly group aged 80 years and older (n = 20, 17.7%) and the aged group aged 60 to 79 years (n = 93, 82.3%)). There were fifty-five male patients (48.7%) in the study. In the very elderly cohort, 80% (n = 16) were female and 20% (n = 4) male as compared to the aged group with 45.2% (n = 42) female patients and 54.8% (n = 51) male. Most occlusions were in the internal cerebral artery in both the very elderly group and the 60-79-year-old groups (75% and 54.8%, respectively). Of the 113 patients, 44 in the 60-79 years old group and 3 in the >80 years old group received tPA as well as ETV. Recanalization was unsuccessful in the very elderly cohort 40% (n = 8) of the time versus

14% (n = 13) in the aged group and they were less likely to attain great reperfusion (TICI score 2b and 3) than the aged group (75.2% vs. 40%, respectively).

The study showed no considerable differences in the rate of complications, i.e., hemorrhage, cerebral edema, or mortality, in either group. On the other hand, infarction progression was witnessed nearly seven times more frequently in the very elderly group with 3 out of 20 patients (15%) than the aged group with 2 out of 93 patients (2.2%). Treatment outcome was assessed at discharge using the mRS. There were worse outcomes in the very elderly group, with poor outcomes (mRS 5–6) in 65% of the very elderly cohort versus 37.6% of the aged patients. The authors concluded these differences were due to EVT being more difficult in the very elderly population due to an increased infarction progression rate and distant occlusion sites.

A multicenter prospective study by Meyer et al. (2020) investigated the outcome and safety of thrombectomy following ischemic stroke in nonagenarians in order to improve decision making in this population (see Table D-4). Data was collected from 25 German institutions between 2013 and 2018. There were 203 patients ≥ 90 years old who met the inclusion criteria for the study. Patients aged ≥ 90 enrolled in the German Stroke Registry Endovascular Treatment (GSR-ET) were combined with a smaller cohort from three additional tertiary stroke centers. (One hundred thirty-nine patients in the GSR cohort and 64 patients who were not part of the GSR group). The inclusion criteria included the diagnosis of AIS due to a large vessel occlusion within the anterior circulation, thrombectomy, patient age ≥ 90 years, and a pre-stroke mRS 0 to 3. Patients under 90 years old were excluded from the study. There were 203 patients with 77.8% (n = 158) women included in the study. A total of 58.6% (n = 119) patients received tPA

prior to thrombectomy. Thirteen patients declined to take part in the follow-up of the study and outcome data was unavailable.

The rate of successful recanalization (TICI ≥ 2b) was 75.9% (n = 154). Patients with successful recanalization (n = 143) had higher rates of good functional outcomes (23.8%, n =34) versus patients with unsuccessful recanalization (14.9%, n =7)]) and lower mortality at 90-days. Of the 193 patients contacted for follow-up, good functional outcome (mRS ≤ 3) was observed in 21.6% (n = 41) at 90-days. In-hospital mortality for the 203-patient sample was 27.1% (n = 55) which increased significantly for the follow-up group (n = 193) at 90 days to 48.9% (n = 93). Symptomatic intracranial hemorrhage occurred in 3% (n = 6) of the total sample of patients. The study showed no differences in outcome between patients treated before registry enrollment and those enrolled in the GSR-ET.

Slawski et al. (2018) completed a multicenter prospective study to evaluate the safety and efficacy of EVT following ischemic stroke in patients 80 years old and over with baseline mRS of 0–4 (see Table D-5). Data was collected from 2015 to 2017 in two Ohio tertiary care centers. Ninety-six patients ≥ 80 years old who received thrombectomy after anterior circulation AIS were included in this study. To meet the inclusion criteria, patients had to be over 80 years old, present with baseline mRS of 0–4 (mild-moderate), and their Alberta Stroke Program Early CT Score (ASPECTS) on non-contrast CT had to be > 6. The patients with severe disability (mRS 5), advanced dementia, and comfort care measures in place were excluded. The 96 patients chosen to be in the study were divided into two groups according to their baseline mRS: 0–1 indicating mild disability (n = 50)

and mRS 2–4 indicating moderate disability (n = 46). The study included more 62.5 % women (n = 60) and a total of 45.8% (n = 44) patients received tPA prior to EVT.

Good outcome (mRS ≤ 2) at 90 days was achieved in 33.7% (n = 32) of the patients with 42.9% (n = 21) in the mild disability group and 23.9% (n = 11) in the moderate disability cohort. The adverse effect of hemorrhagic complication was 37.5% (n = 36), with 6.3% (n = 6) of those patients experiencing symptomatic ICH. The mortality rate was 38.5% (n=37). The rates were considerably higher in the moderate disability cohort in comparison to those in the mild disability group (52.2% vs. 26%, respectively). In this study, one-third of the patients benefited from EVT; however, the best outcomes were seen in the mild disability group who received EVT. Slawski et al. concluded that EVT was a reasonable treatment of AIS in elderly patients.

A multicenter retrospective study was conducted by To et al. (2015) to examine the benefit of thrombectomy following an acute ischemic stroke (Table D-6). Data from patients over the age of 80 in a Michigan institution (Providence Hospital) was collected from 2011 to 2014. There were 2,792 code strokes activated in their health system. Of the 171 patients of all ages who were given tPA, 98 patients underwent thrombectomy. There were 223 patients over 80 years old but only 18 patients met the inclusion criteria for the study; three of these patients received tPA. Fourteen (78%) of the patients were women. The inclusion criteria were age over 80 years, had to have an LVO, and had to received thrombectomy.

Of the 16.6% (n = 3) of patients who received tPA prior to EVT, 66.7% (n = 2) had symptomatic ICH. There was no ICH found in patients who did not receive tPA. Of the 18 patients in the study, 44.4% (n = 8) died. Adverse outcomes were seen in both tPA

and thrombectomy patients. Variables were tested for good or poor outcome association. Female gender was the only variable associated with poor outcome (85.7%, n = 12). A favorable outcome (mRS ≤ 2) was achieved in 27.7%, (n = 5) out of the patients. The authors concluded consideration of the 27.7% good outcome should positively influence the decision to provide EVT to elderly patients. To et al. support EVT in patients over 80 years old because the alternative of not providing thrombectomy could result in an overall detrimental aftermath.

Summary and Conclusions

Stroke is a leading cause of disability and death worldwide. Stroke increases disability in more than half of stroke survivors over the age of 65. Stroke occurs every 40 seconds in the United States and a stroke-related death occurs every three and a half minutes. Although a stroke can occur at any age, the risks increase significantly with advanced age and with risk factors like hypertension, diabetes, atrial fibrillation, smoking and obesity (CDC, n.d.-a). Approved treatments for ischemic stroke currently include intravenous thrombolytics (i.e., tPA) and/or endovascular thrombectomy. It is important to consider the advantages and disadvantages of both treatments in every patient and even more importantly in the elderly population.

This systematic review was conducted to determine if the use of endovascular thrombectomy is recommended for elderly patients over the age of 75 years of age who have suffered an acute ischemic stroke from a large vessel occlusion. The authors of four of the six articles in this systematic review concluded that thrombectomy is safe and effective in patients over the age of 75 years of age who have suffered an acute ischemic stroke from a large vessel occlusion. Despite high mortality rates and less favorable outcomes in the elderly cohorts in their study, the four authors unanimously concluded that the alternative of not providing thrombectomy could have detrimental outcomes. However, the authors of the four articles recommended prudence when considering whether to perform EVT in elderly patients with an acute ischemic stroke from a large vessel occlusion. Thus, every patient and circumstance are different.

Two of the six articles did not specifically state whether or not thrombectomy was effective in elderly patients. Kim et al. (2017) highlighted the difficulties of performing

EVT in elderly patients as a result of an increased infarction progression rate and distant occlusion sites. On the other hand, their study showed no substantial differences in the rate of complications (i.e., hemorrhage, cerebral edema, mortality) in either group. Alawieh et al. (2018) found that age ≥ 80 was associated with increased mortality and poor outcomes after thrombectomy in multiple institutions. This study raised concerns in terms of risk-benefit and cost of performing EVT in elderly patients. Due to the healthcare system's emphasis on cost-effective care, Alawieh et al. (2018) believe there needs to be great improvement in the selection criteria for elderly patients being considered for thrombectomy.

The most significant limitation noted in the six articles was the lack of large elderly cohorts. Due to small sample sizes of the elderly groups, mortality and less favorable outcomes were amplified in comparison to the younger cohorts. In summary, the majority of the articles from this systematic review recommended the use of endovascular thrombectomy for elderly patients over the age of 75 years of age who have suffered an acute ischemic stroke from a large vessel occlusion.

The overall findings of the systematic review suggest the use of endovascular thrombectomy to be effective for elderly patients over the age of 75 years of age who have suffered an acute ischemic stroke from a large vessel occlusion when patient characteristics and comorbities are taken into consideration during treatment decision making.

The limitations of this systematic review were the lack of large elderly cohorts throughout the six studies, the authors' definitions and measurements of good outcomes

were not consistent, and two of the six studies had no conclusion as to whether EVT was effective in elderly patients.

Recommendations and Implications for Advanced Nursing Practice

According to Slawski et al. (2018), by 2050, strokes will more than double, with the greatest percentage of affected patients being over the age of 75. Elderly patients have been known to be excluded from clinical trials solely due to their age and comorbidities (Karhi et al., 2018). Thus, there is limited evidence-based research to assist providers make prudent decisions in regard to performing thrombectomy on elderly patients.

Advanced practice nurses (APRN) and other providers have an obligation to provide care that is safe. Thrombectomy for elderly patients is still a controversial topic in healthcare, thus it is the provider's responsibility to assist patients and families come to the best decision. The articles in this systematic review recommend lifesaving treatments like thrombectomy for elderly patients over the age of 75 who have suffered an acute ischemic stroke from a large vessel occlusion; however, this does not negate the careful considerations which need to be discussed (i.e., preexisting conditions and baseline functionality) for each patient, as every situation is different. Ultimately, the goal is to preserve as much quality of life as possible for these stroke survivors.

APRNs can advocate for and educate their patients and families about the benefits of receiving thrombectomy after suffering an acute ischemic stroke from a large vessel occlusion. In addition, APRNs should educate their colleagues about the evidence regarding thrombectomy in elderly patients and participate in further research about thrombectomy in patients over the age of 75; this is of paramount importance. Strokes will more than double by 2050, with the greatest percentage of affected patients being over the age of 75 (Slawski et al., 2018). APRNs can help bridge the gap in the lack of knowledge regarding EVT in the elderly population.

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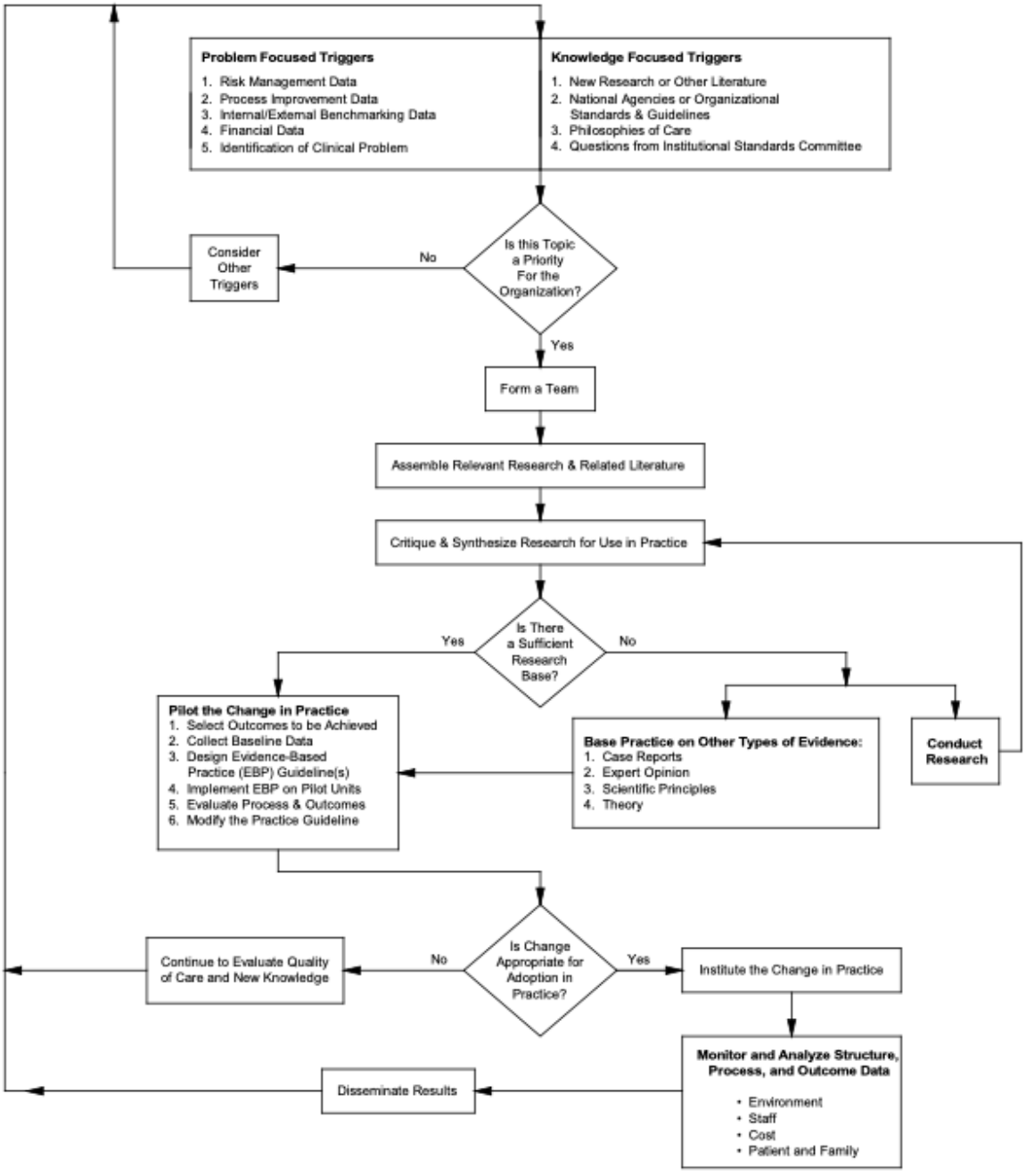
Appendix A

The Iowa Model of Evidence-Based Practice to Promote Quality Care



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REQUESTS TO:
Marita G. Titler, PhD, RN, FAAN
Rhetaugh Dumas Endowed Chair
Dept. Chair Systems, Populations and Leadership
University of Michigan School of Nursing
Ann Arbor, Michigan 48109-5482

Appendix B

PRISMA Checklist (Moher et al., 2009)

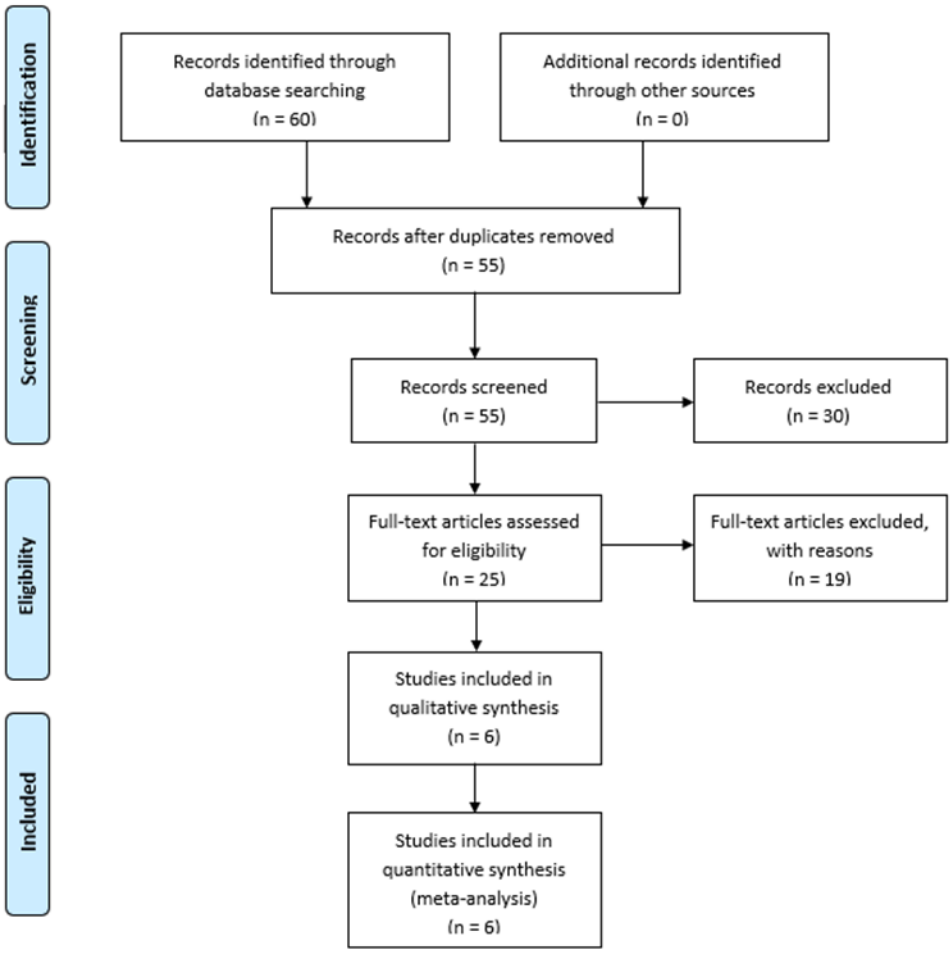
Table 1. **Checklist of Items to Include When Reporting a Systematic Review or Meta-Analysis**

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

Appendix C

Completed PRISMA Flow Diagram

(Moher et al., 2009)



Appendix D
Data Analysis Tables

Table D-1

Alawieh, A., Starke, R. M., Chatterjee, A., Turk, A., De Leacy, R., Rai, A. T., Fargen, K., Kan, P., Singh, J., Vilella, L., Nascimento, F. A., Dumont, T. M., McCarthy, D., & Spiotta, A. M. (2018). Outcomes of endovascular thrombectomy in the elderly: A 'real-world' multicenter study. *Journal of NeuroInterventional Surgery*, *11*(6), 545–553.

Purpose	Design	Site/Sample	Methods	Outcomes Measured	Results	Limitations
To evaluate thrombectomy outcomes in acute ischemic stroke due to large vessel occlusion for patients over and under the age of 80.	Multicenter retrospective chart review.	• Data was collected from seven US-based comprehensive stroke centers between January 2013 and December 2017. • Inclusion: over 18 years old' anterior or posterior circulation stroke, NIHSS recorded at presentation, treated with stent retriever or aspiration thrombectomy as first approach. • Total of 1,442 patients were enrolled. Of these patients, 96 were excluded due to missing demographic information or procedural data. The study proceeded with the remaining 1,346 patients. • Of the 1,346 patients, 346 were over 80 years old. • Of the 1346 patients, 52% were women.	• Patients over the age of 18 years with anterior or posterior circulation ischemic stroke were included. • Patients were separated in to over 80 years old group and under 80 years old group. • Univariate and multivariate analysis were performed to assess the independent effect of age greater than 80 years on outcome predictor. • Subgroup analyses were also performed based on stroke location, recanalization success, or thrombectomy technique used. • The average age in elderly group was 85±5 years compared with 62±13 years in the younger population. • Univariate analysis was used. • There was a higher percentage of women in the elderly group which proved significant. • Treatment with IV tPA was provided to 45.5% of the patients.	• The modified Rankin Scale (mRS) at 90 days was used as the primary clinical outcome. • mRS scores were divided into good outcome (0-2) and poor outcome (3-6).	• Rate of functional independence (mRS 0-2) after thrombectomy was considerably lower in elderly patients. • A direct aspiration first pass technique (ADAPT) was used in 58% of patients and 42% underwent stent retriever thrombectomy as first-line therapy. • 89% had post-procedural reperfusion with TICI ≥2b • A good outcome (mRS 0–2) was observed in 37.5% of cases at 90 days. • 90-day overall mortality was 24.4%. • Overall rate of postprocedural hemorrhage was 31%; rate of PH2-type hemorrhage was 4.4%. • No differences were found between tPA and non-tPA groups. • Age ≥80 was independently associated with increased mortality and poor outcome. • 90-day mortality was significantly higher in the elderly group (35%) versus younger group (20%). • Age ≥80 associated with negative outcome despite thrombectomy technique, stroke location, or success of recanalization. • Age ≥80 independently predicted higher rate of postprocedural hemorrhage (42%) versus age < 80 (28%), but not success of recanalization. • Baseline deficit and number of clot retrieval attempts, were associated with a lower likelihood of good outcome.	• The study was retrospective. • Small sample size and comparison of elderly patients with trial patients.

Table D-2

Karhi, S., Nerg, O., Miettinen, T., Mäkipaakkanen, E., Taina, M., Manninen, H., Vanninen, R., & Jäkälä, P. (2018). Mechanical thrombectomy of large artery occlusion is beneficial in octogenarians. *In Vivo*, *32*(5), 1223–1230.						
Purpose	**Design**	**Site/Sample**	**Methods**	**Outcomes Measured**	**Results**	**Limitations**

To determine if thrombectomy in acute ischemic stroke is beneficial in octogenarians in comparison to younger patients.	Single center retrospective study.	• The study took place in Kuopio University Hospital in Finland between 2009 and 2015.
		• Inclusion: age 18 years or older; LAO in MCA (M1 or M2 segment) or ICA with or without an intracranial thrombus component, confirmed on the admission imaging, available follow-up information for one year after onset.
		• Initially, 261 patients prior to exclusions
		• Of the 261 patients, 199 patients were chosen.
		• 38.2% (n = 76) were female.
		• Group 1: under 80 years old (n = 162).
		• Group 2: 80 years old and over (n = 37).
			• Sixty-two patients were excluded: age under 18 years, posterior circulation occlusion, follow-up data not accessible, secondary stroke occurring as a complication of neurosurgical treatment, and recurrent stroke during the study.
			• The latter group included three patients over 90 years old (91, 92, and 95 years); no upper limit for patient age was set.
			• There was a higher proportion of females (78%) than males (29%) among the octogenarians.
			• Among all patients, the mean age differed significantly between genders.
			  o Females: 72.9 ± 13.9 years.
			  o Males: 63.4 ± 10.8 years.
			• Treatment with IV tPA was provided to 57% of the patients vs. 67%.
			• A single observer, blinded to the retrospective clinical information, evaluated CTA images with the collateral score system:
			  o CS=0: absent collaterals in > 50% of affected M2 vascular region.
			  o CS=1: diminished collaterals in > 50% of M2 region.
			  o CS=2: diminished collaterals in < 50% of M2 region.
			  o CS=3: collateral abundance equal to that on the contralateral side.
			  o CS=4: collateral abundance greater than that on the contralateral side.
				• The modified Rankin scale (mRS) was used to measure the degree of disability.
				• Baseline, imaging, and procedural characteristics, the 3-month modified Rankin Scale (mRS), and 1-year mortality were assessed.
				• Postprocedural reperfusion was considered successful when a TICI score of 2b or 3 was achieved.
					• Successful reperfusion (TICI 2b or 3) was achieved in 75.7% of the older group and 74.7% of the younger group.
					• Older group had more complications during hospitalization (41%) versus younger group (24%), higher 3-month mRS values (4.0 ± 2.3 vs. 2.8 ± 1.9, respectively), fewer favorable mRS values of ≤2 (27% vs. 52%, respectively), higher 3-month (46% vs. 10%, respectively), and 1-year mortality (49% vs. 11%, respectively).
					• Based on a comparison of the mRS measured pre-stroke and at 3 months after the AIS, the older group demonstrated greater deterioration than the younger group.
					• Older group was considerably higher after 3 months.
					• 27% (n = 10) of the older patients achieved a favorable result.
						• Study was retrospectively conducted at one hospital.
						• Sixty-two patients of the 261 that underwent EVT were excluded due to age <18 years old, location of stroke, lack of follow-up data, secondary stroke complications, and recurrent stroke during study.
						• There were only 37 octogenarians in comparison to 162 younger patients.
						• There was a higher proportion of females (78%) than males (29%) among the 80 and over cohort.

Table D-3

Kim, D. H., Kim, S. U., Sung, J. H., Lee, D. H., Yi, H. J., & Lee, S. W. (2017). Significances and Outcomes of Mechanical Thrombectomy for Acute Infarction in Very Elderly Patients: A Single Center Experience. *Journal of Korean Neurosurgical Society*, *60*(6), 654–660. https://doi.org/10.3340/jkns.2016.1212.004.						
Purpose	**Design**	**Site/Sample**	**Methods**	**Outcomes Measured**	**Results**	**Limitations**

To compare the functional outcomes and complication rates in very elderly patients (age ≥ 80 years) and patients (60–79 years) who underwent thrombectomy following ischemic stroke.	Single center retrospective study.	• One hospital in Korea had 171 patients underwent thrombectomy between January 2010 and June 2015.
		• 113 were over age 60 and met inclusion.
		• Exclusion: patients < 60 years old.
		• 17.7% were in the very elderly group, aged ≥80 years (n = 20).
		• 82.3% were in the aged group, aged 60–79 years (n = 93).
		• 48.7% (n = 55) were male.
		• 20% (n = 4) of the very elderly patients, were male compared to (54.8%) in the aged group.
		• Occlusions were mostly in the internal cerebral artery
		  ○ 54.8% in the very elderly group.
		  ○ 75% in the aged group.
		• 41.5 % (n = 47) received tPA.
		  ○ 15% (n = 3) in the very elderly group.
		  ○ 47.3 % (n = 44) in the aged group.
			• Recanalization rates, complications, death, and disability were compared.
			• Univariate logistic regression models were used to evaluate recanalization and clinical outcomes/complications.
			• 41.5% (n = 47) received tPA.
			  ○ 15 % (n = 3) in the very elderly group.
			  ○ 47.3 % (n = 44) in the aged group.
				• Reperfusion was classified by TICI scores.
				• Functional outcomes at discharge were measured according mRS.
					• The NIHSS scores upon presenting to the ER did not differ significantly between the 60–79-year-old group (13.9 ± 6.4) and the ≥80 group (15.6 ± 6.7).
					• 40% (n = 8) of the very elderly cohort versus 14% (n = 13) of the aged cohort and less likely to achieve major reperfusion (TICI 2b or 3) than the younger group (75.2% vs. 40%).
					• There were no considerable differences in the rate of complications, i.e., hemorrhage, cerebral edema, mortality, or re-operation in the post-treatment period.
					• Infarction progression was witnessed seven times more often in the very elderly group (15%, n = 3) than the aged group 2.2% n =2)
					• 65% (n = 13) of the very elderly group had poor outcomes (mRS 5–6) versus 37.6% (n = 35) in aged group.
						• Retrospective study conducted in one institution.
						• Treatment methods and procedures for patients varied; different thrombectomy devices and agents were used. Early in the study, wire-based maceration was mainly used. Later in the study, stent retrievers and balloon guiding catheters were used.
						• The follow-up period ranged from two days to several weeks, which could be too short to accurately assess the results.
						• The Korean Ministry of Food and Drug safety suggested tPA use in patients ≥ 80 years old is contraindicated. This resulted in fewer cases of IV tPA given to the very elderly group.

Table D-4

Meyer, L., Alexandrou, M., Flottmann, F., Deb-Chatterji, M., Abdullayev, N., Maus, V., Politi, M., Bernkopf, K., Roth, C., Kastrup, A., Hanning, U., Brekenfeld, C., Thomalla, G., Gerloff, C., Mpotsaris, A., Papanagiotou, P., Fiehler, J., Leischner, H., Wunderlich, S.,...Limmroth, V. (2020). Endovascular treatment of very elderly patients aged ≥90 with acute ischemic stroke. *Journal of the American Heart Association*, *9*(5), 1–7.						
Purpose	**Design**	**Site/Sample**	**Methods**	**Outcomes Measured**	**Results**	**Limitations**
This study investigates outcome and safety of thrombectomy following ischemic stroke in nonagenarians in order to improve decision making.	Multicenter prospective study.	• In 25 German institutions, 203 patients ≥ 90 years old met the inclusion criteria for the study between 2013 and 2018. • Initially, there were 139 patients in 23 hospitals enrolled; 64 patients were added from three high volume stroke centers. • Inclusion: diagnosis of an AIS attributed to a LVO within the anterior circulation, thrombectomy, patient age ≥ 90 years at the date of treatment, and a pre-stroke mRS 0 to 3. • Exclusion: patients < 90 years old. • 77.8% (n = 158) of patients were women.	• Patients aged ≥ 90 enrolled in the German Stroke Registry Endovascular Treatment (GSR-ET) [n = 139] were combined with a smaller cohort from three additional tertiary stroke centers (n = 64). • 58.6% (n =119) received tPA prior to thrombectomy. Baseline characteristics were compared by using Fisher's exact test for categorical variables, Mann–Whitney U test, and the unpaired Student t test for continuous variables. The Mann–Whitney U test and McNemar test were performed for comparing outcome follow-up data. Univariable regression was followed by multivariable regression analysis to identify independent predictors for good functional outcomes (mRS ≤ 3) at 90- day follow-up.	• Baseline characteristics. • TICI score. • mRS for functional outcomes. • Complications (symptomatic intracranial hemorrhage, serious adverse events).	• Thirteen patients declined to take part in the follow-up of the study and outcome data was unavailable. • The rate of successful recanalization (TICI ≥ 2b) was 75.9% (n = 154). • Patients with successful recanalization had higher rates of good functional outcomes 23.8%, (n = 34) versus patients with unsuccessful recanalization 14.9% (n = 7) and lower mortality at 90-days. • Good functional outcome (mRS ≤ 3) was observed in 21.6% (n = 41) at 90-days. • In-hospital mortality was 27.1% (n = 55) which increased significantly at 90 days to 48.9% (n = 93) of patients not lost to follow-up. • Symptomatic intracranial hemorrhage occurred in 3% (n = 6) of all patients. • There were no differences in outcome between patients treated before registry enrollment and those enrolled in the GSR-ET.	• The study is not generalizable to patients under the age of 90 years. • 6.4% (n = 13) patients declined to take part in the follow-up of the study and outcome data was unavailable retrospectively.

Table D-5

Slawski, D., Salahuddin, H., Shawver, J., Kenmuir, C., Tietjen, G., Korsnack, A., Zaidi, S., & Jumaa, M. (2018). Mechanical thrombectomy in elderly stroke patients with mild-to-moderate baseline disability. *Interventional Neurology*, *7*(5), 246–255.						
Purpose	**Design**	**Site/Sample**	**Methods**	**Outcomes Measured**	**Results**	**Limitations**

To evaluate the safety and efficacy of thrombectomy following ischemic stroke in patients over the age of 80 with baseline modified Rankin Scale (mRS) scores of 0–4.	Multicenter prospective study.	• Ninety-six patients ≥ 80 years old who received thrombectomy after an anterior circulation ischemic stroke in two Ohio tertiary care centers.
		• Inclusion: age ≥ 80, presented with baseline mRS of 0–4 (mild-moderate), taken for thrombectomy.
		• Exclusion: severe disability (mRS5), advanced dementia, and comfort care measures in place.
		• Alberta Stroke Program Early CT Score (ASPECTS) was > 6.
		• Group 1: baseline mRS: 0–1 (n = 50) and group 2 baseline mRS 2–4 (n = 46).
		• 62.5% (n = 60) were women.
		• 45.8% (n = 44) received tPA prior to thrombectomy.
			• ASPECTS baseline mRS were used in determining inclusion criteria.
			• Continuous variables were compared using the Student *t* test with the Welch test or the Mann-Whitney test, and categorical data with the Fisher exact test when it was appropriate.
			• A multivariate logistic regression analysis was completed to assess for clinically significant predictors of favorable outcome.
				• Baseline characteristics.
				• Time to treatment.
				• Rate of revascularization.
				• Procedural complications.
				• Mortality.
				• 90-day good outcome defined as a mRS of 0-2.
					• Recanalization success rate was insignificant between the mild disability group (84.0%) and the moderate disability group (84.8%).
					• Overall hemorrhagic complication rate was 37.5% with 6.3% of the patients experiencing symptomatic ICH.
					• Good outcome at 90 days was achieved in 33.7% (n = 32) of the patients.
					  ○ 42.9% (n = 21) in the mild disability group.
					  ○ 23.9% (n = 11) in the moderate disability group.
					• The overall mortality rate was 38.5% (n = 37). The rates were considerably higher in the moderate disability cohort (52.2%), in comparison to those in the mild disability group 26%.
						• The study was retrospective.
						• There may have been selection bias for patients who presented with less severe symptoms or had advanced dementia.
						• Sample size may have been too small to detect substantial differences between the groups.

Table D-6

To, C., Rajamand, S., Mehra, R., Falatko, S., Badr, Y., Richards, B., Qahwash, O., & Fessler, R. D. (2015). Outcome of mechanical thrombectomy in the very elderly for the treatment of acute ischemic stroke: The real-world experience. *Acta Radiologica Open*, *4*(9), 205846011559942.						
Purpose	**Design**	**Site/Sample**	**Methods**	**Outcomes Measured**	**Results**	**Limitations**
To examine the benefit of thrombectomy following ischemic stroke based on patient outcomes.	Multicenter retrospective study.	• Data from patients over the age of 80 in two Michigan institutions (Providence Hospital and Medical Center). • Inclusion: age over 80 years, LVO, and received thrombectomy. • 2,792 strokes presented from January 2011 to June 2014 of which 223 patients over 80 years old. • 18 patients met the inclusion criteria. • 16.7% (n = 3) received tPA. • 77.8% (n = 14) patients were women.	• Data from strokes meeting inclusion criteria in the Michigan health system institutions from January 2011 to June 2014 were examined (inpatient vs. outpatient strokes were not discussed). • Variables were tested for good or poor outcome association. • All categorical data were analyzed with a chi-square test. Two sample t-tests were used to analyze continuous variables with a normal distribution.	• Physiologic imaging findings. • Use of intravenous thrombolytics. • Baseline and postprocedural NIHSS score. • TICI score. • Functional outcomes (mRS) at discharge and at 90 days. • Discharge destination.	• 66.6% (n = 13) patients had TICI 3 recanalization. • 16.6% (n = 3) patients received tPA prior to thrombectomy. ○ 66.7% (n = 2) of those patients had symptomatic ICH. • There were no ICHs found in patients who did not receive tPA. • 44.4% (n = 8) patients in the study died. • Adverse outcomes were seen in both tPA and thrombectomy patients. • 27.7% (n = 5) had a favorable outcome (mRS ≤ 2). • Female gender was the only variable associated with poor outcome (85.7%, n = 12).	• The study was retrospective. • Sample size may have been too small to detect substantial differences in the results. • 77.8% (n = 14) patients were women.

Appendix E

Critical Appraisal Skills Programme (CASP) Tables

Table E-1

Alawieh, A., Starke, R. M., Chatterjee, A., Turk, A., De Leacy, R., Rai, A. T., Fargen, K., Kan, P., Singh, J., Vilella, L., Nascimento, F. A., Dumont, T. M., McCarthy, D., & Spiotta, A. M. (2018). Outcomes of endovascular thrombectomy in the elderly: A 'real-world' multicenter study. *Journal of NeuroInterventional Surgery*, *11*(6), 545–553.			
A. Are the results of the trial valid?	**Yes**	**Can't tell**	**No**
1. Did the trial address a clearly focused issue?	X		
2. Was the assignment of patients to treatments randomized?	X		
3. Were all of the patients who entered the trial properly accounted for at its conclusion?	X		
4. Were patients, health workers, and study personnel "blind" to treatment?			X
5. Were the groups similar at the start of the trial?			X
6. Aside from the experimental intervention, were the groups treated equally?	X		
B. What are the results?			
7. How large was the treatment effect?	1346 stroke patients		
8. How precise was the estimate of the treatment effect?	($p<0.05$)		
C. Will the results help locally?	**Yes**	**Can't tell**	**No**
9. Can the results be applied in your context?	X		
10. Were all clinically important outcomes considered?	X		
11. Are the benefits worth the harms and costs?			X

Table E-2

Karhi, S., Nerg, O., Miettinen, T., Mäkipaakkanen, E., Taina, M., Manninen, H., Vanninen, R., & Jäkälä, P. (2018). Mechanical thrombectomy of large artery occlusion is beneficial in octogenarians. *In Vivo*, *32*(5), 1223–1230.			
A. Are the results of the trial valid?	**Yes**	**Can't tell**	**No**
1. Did the trial address a clearly focused issue?	X		
2. Was the assignment of patients to treatments randomized?	X		
3. Were all of the patients who entered the trial properly accounted for at its conclusion?	X		
4. Were patients, health workers, and study personnel "blind" to treatment?			X
5. Were the groups similar at the start of the trial?			X
6. Aside from the experimental intervention, were the groups treated equally?	X		
B. What are the results?			
7. How large was the treatment effect?	199 stroke patients		
8. How precise was the estimate of the treatment effect?	($p<0.05$)		
C. Will the results help locally?	**Yes**	**Can't tell**	**No**
9. Can the results be applied in your context?	X		
10. Were all clinically important outcomes considered?	X		
11. Are the benefits worth the harms and costs?		X	

Table E-3

Kim, D. H., Kim, S. U., Sung, J. H., Lee, D. H., Yi, H. J., & Lee, S. W. (2017). Significances and Outcomes of Mechanical Thrombectomy for Acute Infarction in Very Elderly Patients: A Single Center Experience. *Journal of Korean Neurosurgical Society*, *60*(6), 654–660. https://doi.org/10.3340/jkns.2016.1212.004.			
A. Are the results of the trial valid?	**Yes**	**Can't tell**	**No**
1. Did the trial address a clearly focused issue?	X		
2. Was the assignment of patients to treatments randomized?	X		
3. Were all of the patients who entered the trial properly accounted for at its conclusion?	X		
4. Were patients, health workers, and study personnel "blind" to treatment?			X
5. Were the groups similar at the start of the trial?			X
6. Aside from the experimental intervention, were the groups treated equally?	X		
B. What are the results?			
7. How large was the treatment effect?	113 stroke patients		
8. How precise was the estimate of the treatment effect?	($p<0.05$)		
C. Will the results help locally?	**Yes**	**Can't tell**	**No**
9. Can the results be applied in your context?	X		
10. Were all clinically important outcomes considered?	X		
11. Are the benefits worth the harms and costs?	X		

Table E-4

Meyer, L., Alexandrou, M., Flottmann, F., Deb-Chatterji, M., Abdullayev, N., Maus, V., Politi, M., Bernkopf, K., Roth, C., Kastrup, A., Hanning, U., Brekenfeld, C., Thomalla, G., Gerloff, C., Mpotsaris, A., Papanagiotou, P., Fiehler, J., Leischner, H., Wunderlich, S.,...Limmroth, V. (2020). Endovascular treatment of very elderly patients aged ≥90 with acute ischemic stroke. *Journal of the American Heart Association*, *9*(5), 1–7.			
A. Are the results of the trial valid?	**Yes**	**Can't tell**	**No**
1. Did the trial address a clearly focused issue?	X		
2. Was the assignment of patients to treatments randomized?	X		
3. Were all of the patients who entered the trial properly accounted for at its conclusion?	X		
4. Were patients, health workers, and study personnel "blind" to treatment?			X
5. Were the groups similar at the start of the trial?			X
6. Aside from the experimental intervention, were the groups treated equally?	X		
B. What are the results?			
7. How large was the treatment effect?	203 stroke patients		
8. How precise was the estimate of the treatment effect?	(p=0.05)		
C. Will the results help locally?	**Yes**	**Can't tell**	**No**
9. Can the results be applied in your context?	X		
10. Were all clinically important outcomes considered?	X		
11. Are the benefits worth the harms and costs?	X		

Table E-5

Slawski, D., Salahuddin, H., Shawver, J., Kenmuir, C., Tietjen, G., Korsnack, A., Zaidi, S., & Jumaa, M. (2018). Mechanical thrombectomy in elderly stroke patients with mild-to-moderate baseline disability. *Interventional Neurology*, *7*(5), 246–255.			
A. Are the results of the trial valid?	**Yes**	**Can't tell**	**No**
1. Did the trial address a clearly focused issue?	X		
2. Was the assignment of patients to treatments randomized?	X		
3. Were all of the patients who entered the trial properly accounted for at its conclusion?	X		
4. Were patients, health workers, and study personnel "blind" to treatment?			X
5. Were the groups similar at the start of the trial?			X
6. Aside from the experimental intervention, were the groups treated equally?	X		
B. What are the results?			
7. How large was the treatment effect?	96 stroke patients		
8. How precise was the estimate of the treatment effect?	($p<0.05$)		
C. Will the results help locally?	**Yes**	**Can't tell**	**No**
9. Can the results be applied in your context?	X		
10. Were all clinically important outcomes considered?	X		
11. Are the benefits worth the harms and costs?	X		

Table E-6

To, C., Rajamand, S., Mehra, R., Falatko, S., Badr, Y., Richards, B., Qahwash, O., & Fessler, R. D. (2015). Outcome of mechanical thrombectomy in the very elderly for the treatment of acute ischemic stroke: The real-world experience. *Acta Radiologica Open*, *4*(9), 205846011559942.			
A. Are the results of the trial valid?	**Yes**	**Can't tell**	**No**
1. Did the trial address a clearly focused issue?	X		
2. Was the assignment of patients to treatments randomized?	X		
3. Were all of the patients who entered the trial properly accounted for at its conclusion?	X		
4. Were patients, health workers, and study personnel "blind" to treatment?			X
5. Were the groups similar at the start of the trial?			X
6. Aside from the experimental intervention, were the groups treated equally?	X		
B. What are the results?			
7. How large was the treatment effect?	18 stroke patients		
8. How precise was the estimate of the treatment effect?	($p \leq 0.05$)		
C. Will the results help locally?	**Yes**	**Can't tell**	**No**
9. Can the results be applied in your context?	X		
10. Were all clinically important outcomes considered?	X		
11. Are the benefits worth the harms and costs?		X	

Appendix F

Cross Analysis Table

Author, Year	Comparison	Adverse Events	Study Results	Limitations

Alawieh et al., 2018	• Multicenter retrospective chart review in seven US-based comprehensive stroke centers.
	• 1346 patients.
	  ○ 346 were ≥80 years old.
	  ○ 52% were women.
	• Patients ≥ 18 years old with anterior or posterior circulation.
	• Patients were separated into 80 and over year old cohort and under 80-year-old cohort.
	• Patients were treated with stent retriever or aspiration thrombectomy. IV tPA was provided to 45.5% of patients.
		• The rate of functional independence after thrombectomy in elderly patients was considerably lower than for the younger cohort.
		• Age ≥80 was independently associated with increased mortality and poor outcome.
		• Age ≥80 independently predicted higher rate of postprocedural hemorrhage (42% vs 28%).
			• Direct aspiration catheters first pass technique (ADAPT) was used in 58% of patients; the remainder underwent stent retriever thrombectomy as first-line therapy.
			• Post- procedural reperfusion with TICI ≥ 2b was reported in 89% of cases.
			• A good outcome (mRS 0–2) was observed in 37.5% of the cases at 90 days and the overall mortality at 90 days was 24.4%.
			• The overall rate of postprocedural hemorrhage was 31%, and the rate of PH2-type hemorrhage was 4.4%.
			• No differences were found between the tPA and non-tPA groups.
				• The study was retrospective.
				• Small sample size and comparison of elderly patients.

Karhi et al., 2018	• Single center retrospective study in Kuopio University Hospital in Finland. • Of the 199 patients included, 76 were female. • There were 162 patients ≤ 8o years old and 37 patients ≥ 80 years old. • Patients ≥18 years with a LAO in the middle cerebral artery (MCA; M1 or M2 segment) or in the internal carotid artery (ICA). • Treatment with IV tPA was provided to 57% of the patients.	• Based on a comparison of the mRS measured pre-stroke and at 3 months after the AIS, the older group demonstrated greater deterioration than the younger group. • Mortality was considerably higher in the older group than in the younger group after 3 months. • Ten out of the 37 older patients achieved a favorable result.	• Successful reperfusion (TICI 2b or 3) was achieved in 75.7% of the older group and 74.7% of the younger group. • Older patients had more complications than younger group during hospitalization (41% vs. 24%, respectively), higher 3-month mRS values (4.0 ± 2.3 vs. 2.8 ± 1.9, respectively), fewer favorable mRS values (mRS ≤ 2: 27% vs. 52%, respectively), and higher 3-month (46% vs. 10%, respectively) and 1-year mortality (49% vs. 11%, respectively).	• The study was retrospectively conducted at one hospital. • There were only 37 octogenarians in comparison to 162 younger patients. • Sixty-two patients of the 261 that underwent EVT were excluded due to age <18 years old, location of stroke, lack of follow-up data, secondary stroke complications, and recurrent stroke during study.

Author, Year	Comparison	Adverse Events	Study Results	Limitations

Kim et al., 2017	• Single center retrospective study in Korea included 113 patients aged 60 and over.
	• Treatment outcomes were assessed at discharge using the mRS.
	• The study compared the functional outcomes and complication rates in very elderly patients (age ≥ 80 years) and aged patients (60-79 years) who underwent thrombectomy following ischemic stroke.
	• Most occlusions were in the internal cerebral artery in both the very elderly and aged subgroups (54.8% and 75%, respectively).
	• Of the 113 patients, 47 received tPA.
	  ○ 3 in the very elderly group.
	  ○ 44 in the aged group.
		• There were no considerable differences in the rate of complications, i.e., hemorrhage, cerebral edema, mortality, or re-operation in the post-treatment period.
		• Conversely, infarction progression was witnessed almost seven times more often in the very elderly group with 15% (n = 3) of patients than the aged group with 2.25% (n = 2) of patients.
			• The very elderly cohort were approximately three times more likely to have failed recanalization with 40% (n = 8) of patients versus 14% (n = 14) of the patients.
			• The very elderly group was less likely to achieve major reperfusion (TICI score 2b and 3) than the aged group (75.2% vs. 40%, respectively).
			• There were worse outcomes in the very elderly group, with poor outcomes (mRS 5–6) in 65% of very elderly patients versus 37.6% in aged patients.
				• The study was retrospectively conducted in one single institution.
				• Treatment methods and procedures for patients varied as different thrombectomy devices and agents were used.
				  ○ Early in the study, wire-based maceration was mainly used.
				  ○ Later in the study, stent retrievers and balloon guiding catheters were used.
				• The follow-up period ranged from two days to several weeks, which could be too short to accurately assess the results.
				• The Korean Ministry of Food and Drug safety suggested tPA use in patients ≥ 80 years old is contraindicated which resulted in fewer cases of IV tPA given to the very elderly group.

Meyer et al., 2020	• Multicenter prospective study in 25 German institutions. • Included were 203 patients ≥90 years old. • Initially, 139 patients in 23 hospitals were enrolled and then 64 patients were added from three high volume stroke centers. • Inclusion criteria included the diagnosis of an acute ischemic stroke attributed to a large vessel occlusion within the anterior circulation, thrombectomy. • 77.8% (n = 158) were women. • 58.6% (n = 119) of patients received tPA prior to thrombectomy.	• In-hospital mortality for the entire sample was 27.1% (n = 55). • Mortality at 90 days for the sample excluding those lost to follow-up was 48.9% (n = 93). • Symptomatic intracranial hemorrhage occurred in 3% (n = 6) of patients.	• Thirteen patients declined to take part in the follow-up of the study and outcome data was unavailable. • The rate of successful recanalization (TICI ≥ 2b) was 75.9% (n = 154). • Patients with successful recanalization had higher rates of good functional outcomes (23.8%, n = 34) versus those with unsuccessful recanalization (14.9%, n = 7)) and lower mortality at 90-days. • Good functional outcome (mRS ≤ 3) was observed in 21.6% (n = 41) of patients reached for follow-up at 90-days. • In-hospital mortality for the entire sample was 27.1% (n = 55). • Mortality at 90 days for the sample excluding those lost to follow-up was 48.9% (n = 93). • Symptomatic intracranial hemorrhage occurred in 3% (n = 6) of patients. • There were no differences in outcomes between patients treated before registry enrollment and those enrolled in the GSR-ET.	• Study was prospectively conducted. • The study lacked good generalizability due to the exclusion of patients under the age of 90 years old. • Thirteen patients declined to take part in the follow-up of the study and outcome data was unavailable retrospectively. Thus, they were excluded from the final functional outcome analysis.

Author, Year	Comparison	Adverse Events	Study Results	Limitations

Slawski et al., 2018	• Multicenter prospective study in two Ohio tertiary care centers.
	• Study included 96 patients ≥ 80 years old who received thrombectomy after an anterior circulation ischemic stroke.
	• Patients ≥ 80 who presented with baseline mRS of 0–4 (mild-moderate) were included and taken for thrombectomy. Patients with severe disability (mRS 5), advanced dementia, and comfort care measures in place were excluded.
	• Patients were divided into two groups according to their baseline mRS: 0–1 indicating mild disability (n = 50) and 2–4 indicating moderate disability (n = 46).
	• The study included more women than men 62.5% (n = 60).
	• A total of 45.8% (n = 44) patients received tPA before thrombectomy.
		• Hemorrhagic transformation rate was 37.5% (n = 36) with 6.3% (n = 6) of the patients experiencing symptomatic ICH.
		• The overall mortality rate was 38.5% (n = 37). Rates were considerably higher in the moderate disability cohort (52.2%) in comparison to those in the mild disability group (26%).
			• Differences in recanalization success rate was insignificant between mild disability group and moderate disability group (84.0 % vs. 84.8%, respectively).
			• Hemorrhagic complication rate was 37.5%, with 6.3% of the patients experiencing symptomatic ICH.
			• Good outcome (mRS 0-2) at 90 days was achieved in 33.7% of the patients.
			  ○ 43% in the mild disability group.
			  ○ 23.9% in the moderate disability cohort.
			• The overall mortality rate was 38.5%. The rates were considerably higher in the moderate disability cohort, in comparison to those in the mild disability group (52.2% vs. 26% respectively).
				• The study was retrospective.
				• There may have been bias selection for patients who presented with less severe symptoms or had advanced dementia.
				• Sample size may have been too small to detect substantial differences between the groups.

To et al., 2015	• Multicenter retrospective study in a Michigan institution (Providence Hospital) that included patients over the age of 80.
	• There were 2,792 code strokes activated.
	• 223 patients over 80 years old. Only 18 patients over 80 years old met the inclusion criteria for the study (age over 80 years, had to have an LVO, had to received thrombectomy).
	• 16.6% (n = 3) of those 18 patients received tPA.
	• 77.8% (n = 14) of those 18 patients were women.
		• 16.6% (n = 3) patients received tPA prior to thrombectomy
		  ○ 66.7% (n = 2) had symptomatic ICH.
		• 44.4% (n = 8) of the 18 patients in the study died.
		• Adverse outcomes were seen in both tPA and thrombectomy patients. Female gender was the only variable associated with poor outcome (12 out of the 14 women).
			• 66.6% (n = 13) patients had TICI 3 recanalization.
			• 16.6% (n = 3) patients received tPA prior to thrombectomy.
			  ○ 66.7% (n =2) had symptomatic ICH.
			• There were no ICHs found in patients who did not receive tPA.
			• 44.4% (n = 8) of the 18 patients in the study died.
			• Adverse outcomes were seen in both tPA and thrombectomy patients.
			• A favorable outcome (mRS ≤ 2) was achieved in 27.7% (n = 5) patients.
			• Variables were tested for good (mRS ≤ 2) or poor outcome (mRS ≥ 2) association.
			  ○ Female gender was the only variable associated with poor outcome (92%, n = 12).
				• The study was retrospective.
				• Sample size may have been too small to detect substantial differences in the results.
				• 77.8% (n = 14) of the patients in the study were women.