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Research Article

General Anesthesia in the Endovascular Treatment of Acute Stroke: A Prospective, Consecutive, Single-Centre, Interventional Study

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Abstract

Introduction: being debated. General anesthesia in the endovascular treatment of acute ischemic stroke is still

Patients and Methods: A total of 169 patients who met the Safe Implementation of Thrombolysis in Stroke (SITS-MOST) inclusion criteria were admitted to our stroke unit and were treated endovascularily under general anesthesia. Outcome parameters were measured by the modified Rankin Scale as well as theThrombolysis in Cerebral Infarction (TICI) scale score. Follow-up evaluations were made at discharge and also at 90 days. All complications were registered.

Results: The rate of successful re-canalization for patients treated under general anesthesia was 69%, the mean time from symptom onset to groin puncture was 221 (77-679) minutes and the time delay from induction of anesthesia to groin puncture was 35 (10-115) minutes. At 90 days 43% of observed patients were documented with good clinical outcome. The mortality rate was 17%.

Conclusion: Endovascular treatment under general anesthesia even with an acceptable time delay is feasible in well organized stroke centers and may provide better procedural conditions than conscious sedation.

Keywords: Ischemic stroke; Endovascular treatment; General anesthesia; Conscious sedation; Thrombectomy

Key Points

GA for endovascular treatment for ischemic stroke is still being debated.

The advantage of GA is that the movement of the patient is eliminated. GA therefore allows greater procedural accuracy and reduces the risk of procedural complications.

The time delay involved with GA is acceptable in well-organized stroke centers.

A prospective, randomized study may show if GA has a better outcome than CS.

Abbreviations

General Anesthesia (GA), Conscious Sedation (CS), Thrombolysis in Cerebral Infarction (TICI), Endovascular Mechanical Re-canalization (EMR).

Introduction

Stroke management has evolved rapidly in the past decade. Still stroke is one of the three leading causes of death and life-long disability worldwide [1,2].

Intravenous thrombolysis (IVT) using recombinant tissue plasminogen activator is often fails in re-opening large cerebral artery occlusion [3].

Therefore endovascular mechanical re-canalization (EMR) techniques are gaining importance

There is still a serious debate among neuro interventionalists whether patients should receive general anesthesia (GA) or conscious sedation (CS) for EMR [4-8]. The main argument against GA is the time delay until groin puncture [9].

In this analysis we will show the thrombectomy results we obtained from all our patients only treated under GA.

Materials and Methods

Study population

All 169consecutive patients admitted to our stroke unit from February 2007 to May 2013 who were treated with EMR were registered in the Stroke Unit registry, a nationwide database.

The most recent thrombectomy devices were used as soon as they became available.

Clinical outcome parameters were measured by the National Institute of Health Scale (NIHSS) at time of admission and discharge. Information on functional outcome, assessed by the modified Rankin Scale (mRS), was measured at 90 days after treatment. Time of symptom onset to admission, time from admission to first

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neuroimaging and the door-to-needle-time were assessed.

Radiological investigations

All patients underwent computed tomography (CT) scan including a computed tomography angiogram (CTA) at admission. In case of allergy to iodine magnetic resonance imaging (MRI) with diffusion weighted sequences (DWI) and magnetic resonance angiography (MRA) was performed. Patients with undefined symptom onset or with strokes out of the intravenous time window were treated with EMR only with a proven mismatch in MRI. [10,11] Large cerebral artery occlusion was defined as complete obstruction of the flow in the internal carotid artery (ICA), middle cerebral artery (MCA) or basilar artery (BA). The first post procedural CT was always obtained within 24 hours or immediately, if any clinical deterioration was observed.

Reperfusion was measured by the Thrombolysis in Cerebral Infarction (TiCI) scale [12,13]. Successful re-canalization was defined as a score of 2b and 3 on the TiCI.

Treatment

Patients admitted to our stroke unit were monitored and received prophylaxis for deep-vein thrombosis, according to the stroke guidelines [3]. If patients meet the inclusion criteria according SITS-MOST, IVT is indicated within a time window of 4.5 hours after symptom on set and in tra-arterial thrombolysis (IAT) within 6 hours [14,15]. In our internal guidelines for IAT and EMR, we extended the time window up to 12 hours in patients with basilar artery (BA) occlusion. If unconsciousness had lasted less than 4 hours and in case of patients with fluctuating symptoms, we even extended the time window to 24 hours.

If indicated, patients were transferred immediately to the angiography suite under ongoing IVT as a bridging therapy.

Anesthesiological considerations

The team of anesthesiologists was alarmed in advance before the stroke patient´s arrival at the hospital. GA was performed only by neuroanesthesiolgists on request of the surgeon. The reasons for GA were to avoid unforeseeable movements, to improve the oxygen supply of the patient as well as the comfort of the patient concerning long lasting motionlessness. Furthermore stroke patients frequently do not obey simple commands, breathe shallowly and they are anxious. In the majority of cases they are also not cooperative.

There was of course no fastening prior to anesthesia. Therefore crush induction in a 30°-45° upper part elevated position was necessary. With intention to avoid a drop of blood pressure phenylephrine 10mg dissolved in 500ml saline was administered by electronic infusion device before induction of general anesthesia in all patients [16] Patients were preoxygeneted via face mask until an expiratory oxygen concentration higher than 90% was reached. After injecting fentanyl 0.15 $\mu g kg^{-1}$, propofol was given until the eyelash reflex disappeared. Intubation was performed under relaxation by rocuronium 1.2 $mg kg^{-1}$ based on ideal body weight. Insertion of a cannula in the radial artery was mandatory for beat to beat measurement of blood pressure. Hypotension was treated in all patients with fluids and phenylephrine to achieve a systolic blood pressure of at least 150mmHg and a mean arterial pressure of at least 100 mmHg during the entire procedure until clot removal [16]. Anesthesia was maintained with sevoflurane MAC 1. Analgesia was provided by fentanyl boluses depending on increase of heart rate. With the intention to maintain sufficient cerebral perfusion patients were ventilated to an $EtCO_2$ between 35 and 40 mmHg [17]. SpO_2 higher than 98%wasdesired.Systolic blood pressure was kept between 110 and 130 mmHg by titrating urapidil 10mg stepwise after successful re-canalization to avoid hyper perfusion injury [18]. A warming mattress was used to prevent excessive decline of body temperature below 34°C. Postoperative pain caused by compression bandages was treated prophylactically with 1000 mg paracetamol. After vessel reopening, patients were extubated in the neurological intensive care unit immediately after re-warming.

Endovascular procedure

Digital subtraction angiography was performed on a biplane high-resolution angiography system (Art is Zee Biplane System, Siemens AG, Germany) via a femoral approach. All procedures were performed by two neuro interventionalists.

We used either a 6F or 8F guide catheter or in cases of very twisted vessels, a 6F or 8F long sheath to reach the target artery. Occlusion of the target vessel was verified angiographically and rated on the TICI scale. Using a coaxial system, we advanced a distal access catheter and a microcatheter over a guidewire placed through the thrombus. After removal of the guidewire, a microcatheter angiographic run was performed to confirm the correct positioning. Then the retrieval device was advanced through the microcatheter across the vessel occlusion and deployed completely by pulling back the microcatheter. The distal access catheter was positioned as distal as possible, preferably in the M1 segment regarding MCA occlusions and next to the occluded part of the basilar artery regarding basilar artery occlusions. The device was then removed into the distal access catheter, while applying suction through the distal access catheter. An angiographic run was performed to evaluate flow restoration. If necessary, the entire process was repeated until the end of the therapeutic window. Groin punctures were routinely closed with a closure system.

Endovascular retrieval devices were used chronologically as they were available.

During the endovascular procedure, the following time points were documented: time from start of intravenous thrombolysis to start of general anesthesia, time from symptom onset to groin puncture, time from first neuroimaging to groin puncture, time from start of general anesthesia to groin puncture, time from groin puncture to first angiography of the target artery, time from target artery to first micro-angiogram, time from first micro angiogram to termination, time from symptom onset to first usage of the microcatheter, time from groin puncture to termination of angiography, time from symptom onset to termination, and time from arrival to termination.

Post-interventional management

If there was no contraindication revealed by a CT scan undertaken 24 hours after the operation, oral medication with acetyl salicylic acid 100mg was started on the first day after the procedure. All patients were checked by MR scan before discharge or Trans feral.

Complications

An intracerebral hemorrhage (ICH) was defined as symptomatic,

Table 1: Demographic data and radiological findings.

age	66 (27-90)
men	56% (95/169)
women	44% (74/169)
Basilar artery	18% (30/169)
middle cerebral artery	61% (103/169)
Carotis artery occlusion	21% (36/169)
TICI score 1 at admission	100%
TICI score at discharge	
TICI 1	11% (18/169)
TICI2 a	19% (32/169)
TICI 2b	29% (49/169)
TICI 3	41% (70/169)
TICI 2b and 3	70% (119/169)
One step recanalization	20% (33/169)
Distal embolization	1% (2/169)
Vesselperforation	2% (4/169)
Symptomatic ICH	12% (20/169)
Asymptomatic ICH	29% (49/169)
Malign Infarction	9% (16/169)

when an increase of 4 or more points in the NIHSS score occurred within 24 hours in concordance with the evidence of any blood on the 24-hour head CT/MRI scan. Patients detected with asymptomatic ICH were registered with a small subarachnoidal hemorrhage or hemorrhage in the infarction area without clinical deterioration. According to the SITS-MOST criteria a symptomatic bleeding was defined with a hemorrhage in the infarct area that causes a mild to substantial space-occupying effect. Intracerebral hemorrhagic transformation in the infarction area without clinical deterioration was defined as asymptomatic [19].

Statistical analysis

Data were carefully checked for possible outliers. Descriptive analyses were done by computing means, range, and relative percentages.

Results

All 169 patients were treated with GA.

Demographic data and radiological findings are listed in (Table 1).

61% of treated patients received intravenous thrombolysis either before or before and during the procedure (Table 2).

The mean time from start of GA to groin puncture was 35 (10-115) min. Mean treatment time (groin puncture to procedure termination) amounted to 88 (10-185) min. Further intervals and performed options of treatment are shown in (Tables 3,4).

The types and the frequency of used devices are mentioned in (Table 5).

Successful re-canalization TICI 2b and TICI 3 was achieved in 69% of cases. Clinical outcome was good, resulting in am RS score ≤2 in 43% of patients. We did not use balloon guide catheters for distal embolization protection. The distal access catheter was positioned as distal as possible. As we performed at the distal access catheter suction during the stent retrieval procedure, we did not experience distal embolization (Table 2).

Table 2: Intravenous thrombolysis either before or before and during the procedure.

NIHSS at admission	18 (Fass Dr. Wintersteller28)
intravenousthrombolysis	61% (103/169)
additional intraarterial rt-PA	48% (81/169)
NIHSS discharge	12 (0-26)
mRS discharge	
mRS ≤2	23% (39/169)
mRS 3	20% (33/169)
mRS 4+5	45% (76/169)
mRS 6 = deceased	12% (21/169)
mRS at 90 days	n=148
mRS ≤2	48% (71/148)
mRS 3	17% (25/148)
mRS 4+5	28% (41/148)
mRS 6 = deceased	5% (8/148)
lost	2% (3/148)
Overall deceased	17% (29/169)

Symptomatic ICH occurred in 12%, asymptomatic ICH in 29%, and vessel perforation in 2% (Table 1).

The overall mortality rate was 17% at 90 days. Further data of outcome are summarized in (Table 2).

Discussion

The management of acute ischemic stroke has evolved in the last decade because large clinical trials have shown the efficacy of mechanical re-canalization devices in large cerebral artery occlusion [9,13].

A total of 70% of all patients treated with EMR under GA were found to have successful re-canalization.

Various types of sedation are now used in acute ischemic stroke [4-8]. There is a controversy about whether to use GA or CS during the endovascular treatment of acute ischemic stroke. Current data only provide little information concerning thrombectomy under GA or CS. Another drawback of these studies is that different time gaps have been analyzed, as far as the individual procedures used on a stroke patient between admission and arrival in the endovascular ward.

The main concern against using GA is the time delay until the start of the neuro interventional procedure itself [14].

Studies have revealed that the duration of the time delay is influenced by the availability of anesthetic staff [17].

We registered a mean time delay from symptom onset to the first

Table 3: Time gaps of symptoms onset and procedures in minutes mean and range (n = 169).

Symptom onset to intravenous thrombolysis	120 (48-715)
Symptom onsettoadmission	114 (20-717)
Hospital admission to first CCT	22 (2-86)
First CCT prior to intravenous thrombolysis	20 (3-160)
Doortoneedle time	43 (14-99)
Start anesthesia to groin puncture	35 (10-115)
Symptom onset to groin puncture	221 (77-679)
Groin puncture to first target vessel	18 (2–115)
Target vessel to first microcatheter	29 (22-101)
Microcatheter to recanalization/ procedure termination (min)	40 (3-100)
Target vessel to recanalization/termination (min)	63 (9-142)
Groin puncture to procedure termination	88 (10-185)

Table 4: Interventions and drug therapy (n = 169).

Intra-arterialthrombolysis	81 (48%)
Stent	25 (15%)
No EMR (no access possible)	3 (2%)
Intravenousthrombolysis	103 (61%)
Tirofibanadministered	25 (15%)
Intermediate catheter	70 (41%)
Decompressivesurgery	13 (8%)

procedure, the groin puncture, of 222 min, which is much shorter than the previous studies, reported. Abou-Chebl, et al. analyzed 980 patients treated with IAT and showed a mean time delay in patients treated under GA of 306 min, and under CS of 296 min [20]. Another trial, which analyzed 126 thrombectomy patients, documented a mean time delay of 417 min in patients treated under GA and even in patients treated under CS a mean time delay of 654 min [21]. A retrospective analysis of 66 Merci retriever treated patients, registered a mean time delay of 271 min in patients treated under GA and 260 min in patients treated under CS [22].

The two stent retriever trials, Trevo 2 and Swift, did not differentiate in their analysis between patients treated under GA or CS. Overall, Trevo 2 showed a mean time delay form symptom onset to groin puncture of 300 min (82% within88 Trevo treated patients received GA) and Swift reported 31 patients with a mean time delay of 301.6 min [13,23].

Hassan, et al. registered the time from arrival to microcatheter positioning and described 53 endovascularily treated patients under GA with a mean time delay of 310 min and 83 patients treated under CS a mean time of 287 min [24]. We found a mean time of 262 min, even shorter than the results of Hassan, et al. Our shorter time delay may be because we have a team of anesthesiologists experienced in stroke patients available 24 hours every day. These neuro anesthesiologists are so experienced that they avoid significant alterations in hemodynamic parameters and cerebral perfusion pressure during the induction of GA and so avoid damage of the ischemic penumbra, which reacts very sensitively to hemodynamic changes [25]. A specialized stroke neurologist receives the stroke patients as soon as they arrive at our institution. Another important fact is that the emergency room of our institute and the staffroom of the anesthesiologists are located very close to the radiological department and the endovascular suite. Stroke patients are treated immediately after arrival without any waiting time.

The mean time delay between acute stroke imaging and the first angiographic run was 87 min. Berkefeld; et al. documented a mean time delay of 50 min for 31 patients treated endovascularly under GA and a mean time of 65 min within 9 patients without GA [14].

The inclusion of tele stroke patients in our data may have reduced the time delay by 20 to 30 minutes.

As described before, the time from symptom onset to groin puncture in our data is comparable to former studies that analyzed endovacularily treated patients under CS, even shorter.

The performance of thrombectomy under GA has many advantages. The main advantage is the elimination of movement of the patient, which allows a greater procedural accuracy, reduced time delay, and a potentially reduced risk of procedural complications [14].

The mean procedure time from groin puncture to re-canalization in our study was 88 minutes, which is significantly better than studies that showed a mean procedure time of 111 minutes for 57 and 99 minutes for105 endovascularily treated patients under CS [26,27] Similar findings and even lower procedure times compare favorable to former thrombectomy studies that also treated patients under GA [13,28,29].

It is known that the insertion of the Endoluminal device into the intracranial vessels and the process of clot retrieving are associated with discomfort and even pain. The advantage of GA is the prevention of intra-procedural pain thereby also reducing the risk of patient agitation and restlessness [30,31].

The movement of the patient disrupts the roadmap, thus increasing the risk of complications such as perforation [32]. Only 2% of all analyzed patients were documented with vessel perforation because GA eliminated patient movement.

Endovascular treatment under GA further ensures airway protection and obviates the need for emergency conversion to GA. Acute stroke patients are unlikely to have adequately fasted and are at high risk of pulmonary aspiration. Furthermore most severely affected stroke patients suffer from dysphagia and may be unable to protect their airway themselves [33]. Many studies described the urgent need to conversion to GA during the endovascular procedure under CS [26-20,34,35].

The relatively short time delay needed for GA seems to be acceptable because the intervention can be performed under optimal conditions, as fast as possible, and with a high technical success rate [14]. Furthermore the MRCLEAN study shows that the effect of treatment as a risk difference on reaching independence is influenced by the time taken until reopening of the vessel occlusion and not by the time of the onset of the symptoms to groin punctures [9].

The rate of symptomatic hemorrhage was 12%, equal to former studies. The Multi Merci Trial registered symptomatic hemorrhage rate of 10% for 111 patients and as tent retriever study showed a hemorrhage rate of 15% for 101 patients treated [36,37]. Castagno, et al. also analyzed 20 patients treated under GA with a symptomatic hemorrhage rate of 10% [29].

Trevor 2 included 82% of 88 patients treated end avascularity under GA and even showed a symptomatic ICH rate of 7% [23]. In a study with 980 patients, Abou-Chebl, et al. found no significant differences in patients treated with GA in comparison to those treated only with CS (9.3% *vs.* 9.1%; p=<0.82) regarding the hemorrhage rate [38]. Concluding that treatment under GA does not cause a higher hemorrhage rate, but rather it reduces bleeding events due to better surgical conditions [14]. Numerous studies have suggested GA to be independently associated with poorer outcomes during the neuro interventional procedures [38,34,4,39] Nichols, et al. postulated that deep sedation is associated with increased mortality [4].

Most studies that compared endovascular treatment under GA to CS documented higher baseline NIHSS in patients treated under GA than CS, and therefore recommended endovascular treatment under CS to achieve a better clinical outcome [38,34,25].

43% of our patients were documented with good clinical outcome, similar or even higher rates compared favorably to other stent retriever studies that documented comparable rates of re-vascularization outcomes ranging from 30%-54% at day 90 [4,36,40-43].

This is lower than in studies in which patients were treated under CS, as can be seen in studies in which the mortality rate of 66 endovascularity treated patients was 29.8% and with 36 endovascularily treated patients, 22.2% and with 126 similarly treated patients were 22.2% [25].

Similar to our results, stent retriever studies reported mortality rates ranging from 7% to 33% [23,36,41,44]. Our data did not confirm GA to be associated with a higher mortality rate. As mentioned before the procedure seems to be more accurate under GA.

In contrast to van den Berg, et al. who reported a good clinical outcome mRS ≤ 2 in 26% of patients in non-GA group and in 14% of patients in GA group, we achieved a good clinical outcome in 43% of patients [45]. All of them were treated under GA. The mortality rate, 17% in our study, was equal to the non-GA group and even better than GA group at 21%. This might be explained by our standardized regime of GA, which avoided long lasting decrease of blood pressure, low tension of carbon dioxide, and hypoxemia. Insufficient oxygenation occurs in slowly and shallowly breathing patients under CS. Furthermore our study showed a more frequent angiographic reperfusion TiCI 2b/3b 69% versus 43% in non-GA group and 49% in GA group.

Our study had two limitations. First, the number of patients was small. Second, we did not have a control group which received endovascular treatment under CS.

Only centers that provide experienced anesthesiologists 24 hours every day without any waiting time for them should perform endovascular treatment under general anesthesia. Our and Brekenfeld´s data show that GA can be performed with an acceptable time delay in well-organized stroke centers [14].

Our data may go with Schönenberger´s findings which do not show any advantage of CS although anesthesiology procedures were not standardized in this study [45].

As recommended in several recently published articles, a prospective, randomized study is needed to show any difference in neurologic outcome between patients treated either by GA or by CS for EMR [46-49].

Conclusion

Endovascular treatment under GA is feasible with an acceptable time delay in well organized stroke centers. Endovascular treatment under GA has the advantage of optimal surgical conditions, fewer technical failures, best patient monitoring, airway protection, and may also have better clinical outcomes caused by acceptable re-canalization results.

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