Thrombectomy in Childhood Stroke

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Background—Several randomized trials have shown the efficacy of thrombectomy for large intracranial vessel occlusions in adults. However, the safety and efficacy of thrombectomy in children are unknown. We aimed to investigate the feasibility and outcome of thrombectomy in pediatric patients.

Methods and Results—We performed a retrospective analysis of all children (<18 years of age) who presented with large-vessel occlusion and were treated with mechanical thrombectomy at 3 German tertiary-care stroke centers. Interventional results and clinical outcomes were assessed using the Pediatric National Institutes of Health Stroke Scale at 24 hours and on day 7 after thrombectomy as well as after 3 months (modified Rankin Scale). After screening of local registries for all performed thrombectomies, 12 children were included. Median Pediatric National Institutes of Health Stroke Scale score on admission was 12.5 (interquartile range 8.0-21.5). Angiographic outcomes for thrombectomy were good in all patients (6×modified Treatment in Cerebral Infarction Score 3, 6×modified Treatment in Cerebral Infarction Score 2b). Moreover, most patients showed an improvement of neurological outcome after thrombectomy with a median Pediatric National Institutes of Health Stroke Scale of 3.5 (interquartile range 1-8) at day 7 and a modified Rankin Scale of 1.0 (interquartile range 0-2.0) at 3 months. No major periprocedural complications were observed.

Conclusions—In our retrospective study thrombectomy was safe in childhood stroke, and treated children had good neurological outcomes. **(*J Am Heart Assoc.* 2019;8:e011335. DOI: 10.1161/JAHA.118.011335.)**

Key Words: ischemic stroke • thrombectomy • ischemic stroke • childhood stroke • pediatric stroke • endovascular recanalization

Childhood stroke with an estimated incidence of 2 to 8 per 100 000 children per year is a rare clinical event with potentially severe outcome.[1] Several randomized trials have shown the efficacy of thrombectomy for large intracranial vessel occlusions in adults and have provided clear evidence for improved neurological outcome compared with intravenous thrombolysis alone.[2-4] However, the safety and efficacy of thrombectomy in children are unknown, and only a few reports have described technical considerations as well as potential risk factors.[5-8] Moreover, etiologies vary considerably between childhood and adult stroke.

Because large prospective clinical trials are unlikely to be feasible in children, we present a multicenter series of pediatric patients treated with thrombectomy for ischemic stroke.

Methods

Imaging data are not available to researchers. Summary data and methods are available from the corresponding author on reasonable request.

We performed a retrospective study including all children (<18 years of age) presenting with acute ischemic stroke due to large vessel occlusion of the anterior circulation and who were treated by mechanical thrombectomy between January 2013 and December 2017 at 3 German tertiary-care stroke centers. Patients were identified by searching the radiological databases and operation procedure codes of the participating centers for all children who presented with ischemic stroke.

The study was approved by the Ethics Committee of the University of Muenster, and the requirement for informed

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consent was waived. All study protocols were conducted in accordance with the Declaration of Helsinki.

Intervention and Imaging

All patients underwent NCCT (non-contrast computed tomography), CTA (computed tomographic angiography), and CTP (computed tomographic perfusion) on admission. All computed tomographs (CTs) were performed on multislice detector CT scanners (Somatom and Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany), and CTP postprocessing was performed using commercially available Siemens software (syngo.via, Siemens, Forchheim, Germany). The size of the penumbra was determined from the volume of tissue at risk beyond the volume of early infarct. Tissue at risk and early infarct in CTP were estimated visually using quantitative cerebral blood flow and cerebral blood volume perfusion maps, respectively. Any cerebral blood flow lesion of ≈30 mL/(100 g·min) or less was defined.

In general mechanical thrombectomy was favored if the patient presented within the time window of 6 hours after the onset of symptoms, showed no or minor infarction on noncontrast CT scan, and had a clear mismatch in the CT perfusion study as well as a vasculature that permitted the insertion of at least a 5Fr-sized catheter armamentarium. However, the final decision in each individual case was always at the discretion of an interdisciplinary team of neuropediatricians, neuroradiologists, and neurologists.

Mechanical thrombus removal was performed in all cases via stent retrievers; in 5 cases additional contact aspiration was performed. Thrombectomy was performed in all cases through a transfemoral approach. Either 6F or 8F sheaths and guiding catheters were used depending on the size of vasculature. Thrombectomy was performed in all cases using stent retrievers sized 4×20 mm (Phenox Preset, Bochum, Germany; Solitaire Medtronic, Minneapolis, MN; Trevo Stryker Neurovascular, Fremont, CA). Up to 3 passes were required to clear the target vessel from the occlusion. In 5 cases additional contact thrombus aspiration was performed using a 6F aspiration catheter (Ace 64, Penumbra, Alameda, CA). No intravenous or intraarterial thrombolysis was applied, nor was periprocedural heparin. To obtain hemostasis at the end of the procedure, vascular closure devices were applied in all patients, followed by a compression bandage for 6 hours.

ASPECT (Alberta Stroke Program Early CT) scores on admission and follow-up imaging were assessed as part of our routine stroke diagnostics by experienced neuroradiologists at the time of initial CT reading. A Modified Rankin Scale score was calculated retrospectively by the authors based on clinical descriptions in the medical chart, blinded to the clinical and radiological severity of the initial infarct.

Statistics

Patient demographics, procedural characteristics, and outcome are reported as median (interquartile range) and total range or as frequency.

Results

Study Population

Of a cohort of 158 children presenting with ischemic stroke, all children treated with thrombectomy due to anterior circulation stroke at our centers during the study period were included, resulting in a total of 12 children (7.6%) (Table 1); the median age was 14 years (interquartile range 7.8-16, total range 5-17 years). None of the patients received intravenous thrombolysis before intervention. Five children suffered from congenital heart disease, 2 patients were affected by focal cerebral arteriopathy of the inflammatory subtype (diagnosed later in the course after mechanical recanalization), and 1 patient each suffered from sepsis-associated coagulopathy, thalassemia, fibromuscular dysplasia, secondary vasculitis after meningitis, and carotid artery dissection. All 5 children with underlying cardiac anomaly had been under oral anticoagulation therapy with warfarin before the ischemic stroke.

We have not systematically evaluated children with large-vessel occlusion not treated with thrombectomy. However, recorded reasons why pediatric patients did not receive endovascular treatment include substantial infarction of the middle cerebral artery territory on admission, occlusion of the M2 segment of the middle cerebral artery with a diameter too small for thrombectomy, and known vasculitis associated with high-grade vessel stenosis.

Angiographic and Clinical Outcome

Angiographic outcomes for thrombectomy were good in all patients (6×modified Treatment in Cerebral Infarction Score [TICI] 3, 6×modified TICI 2b). Moreover, most patients showed an improvement of neurological outcome after thrombectomy: median Pediatric National Institutes of Health Stroke Scale on admission was 12.5 (interquartile range 8.0-21.5), and median Pediatric National Institutes of Health Stroke Scale at day 7 after the intervention was reduced to 3.5 (interquartile range 1-8) (Table 1).

Only 1 patient showed a poor outcome (modified Rankin Scale 3), even though angiographic outcome was initially good (modified TICI 2b). This patient had hypoplastic left heart syndrome and suffered a contralateral thromboembolic stroke 1 day after the successful first thrombectomy. This patient showed clear infarct demarcation on follow-up NCCT (non-

Table 1. Patient Characteristics

Characteristic	Total (n=12)
Male/female	6/6
Age, y	
Median and interquartile range	14 (7.8-16)
Total range	5 to 17
Onset of symptoms to thrombectomy, h	
Median and interquartile range	2.0 (2-3)
Total range	1 to 4
Onset of symptoms to diagnosis, h	
Median and interquartile range	1.5 (1.1-2.0)
Total range	0.5 to 3
Diagnosis to thrombectomy, h	
Median and interquartile range	0.5 (0.5-0.9)
Total range	0.5 to 1.0
CT+CTA pre	12/12
Arterial occlusion (ICA+M1/M1/M2)	2/9/1
ASPECT Score pre*	
Median and interquartile range	8.0 (7.0-8.8)
Total range	6 to 10
ASPECT Score post*	
Median±SD	7.5 (6.3-8.0)
Total range	2 to 9
PedNIHSS pre†	
Median and interquartile range	12.5 (8.0-21.5)
Total range	3 to 33
PedNIHSS 12 to 24 h post†	
Median and interquartile range	4.0 (1.0-7.8)
Total range	0 to 10
PedNIHSS 7 days post†	
Median and interquartile range	3.5 (1-8)
Total range	0 to 15
mTICI (0/I/IIa/IIb/III)‡	0/0/0/6/6
Modified Rankin scale score at 3 mo§	
Median and interquartile range	1.0 (0-2.0)
Total range	0 to 3
PSOM at 3 mo‖	
Median and interquartile range	1.0 (0-3.0)
Total range	0 to 5
Follow-up CT within 1 wk	12/12
Etiology	
Cardiac	5
FCAi	2
Coagulopathy	2
Secondary vasculitis	1
Dissection	1
Fibromuscular dysplasia	1

CT indicates computed tomography; CTA, computed tomographic angiography; FCAi, focal cerebral arteriopathy of inflammatory subtype; ICA, internal carotid artery; M1 and M2, middle cerebral artery segments M1 and M2; mRS, modified Rankin Scale; PedNIHSS, Pediatric National Institutes of Health Stroke Scale; post, 12–24 hours after admission; pre, on admission.
*The ASPECTS (Alberta Stroke Program Early Computed Tomography Score) is an imaging measure of the extent of ischemic stroke. Scores range from 0 to 10, with higher scores indicating a smaller infarct core.
†Scores on PedNIHSS range from 0 to 42, with higher scores indicating more severe neurologic deficits.
‡Modified Treatment in Cerebral Infarction Score (mTICI) reaches from 0 (no reperfusion) to 3 (complete reperfusion).
§Scores on the modified Rankin Scale (mRS) of functional disability range from 0 (no symptoms) to 6 (death). A score of 2 or less indicates functional independence.
‖Scores on Pediatric Stroke Outcome Measure (PSOM) range from 0 to 10, with higher scores indicating more severe neurologic deficits.

contrast computed tomography) (ASPECTS 2). All other patients revealed either no or minor signs of cerebral infarction (Table 1). Of note, no infarct-associated hemorrhage was observed.

Altogether, our patients had no complications after thrombectomy other than transient periprocedural vasospasm, detected angiographically, which occurred in 2 patients. A 7-year-old boy suffered from a complex cardiac anomaly and showed transient vasospasms of the middle cerebral artery territory after TICI 2b recanalization of an M2 occlusion. A 14-year-old boy affected by vasculitis also showed transient vasospasms in the middle cerebral artery territory after TICI 3 recanalization of a carotid-T occlusion. In both cases the vasospasms resolved completely and without any clinical sequelae after administration of nimodipine (see also Table 2). No vascular complications such as arterial dissection, periprocedural thrombosis, or puncture site complications occurred. After mechanical thrombectomy 10 of 12 patients were put on low-molecular-weight heparin for recurrence prevention.

Discussion

Endovascular thrombectomy has emerged as the standard of care for adult patients with acute ischemic stroke due to large-vessel occlusion.[2-4] The knowledge about efficacy and safety of mechanical recanalization in childhood stroke, however, is limited to small patient series and case reports. These existing case reports have been well summarized,[6,8] but the potential to apply this technique in pediatric patients has not yet been explored systematically.

Table 2. Individual Patient Characteristics

Age, y	Sex (M/F)	Thrombus Location	Etiology	Time From Onset of Symptoms to Diagnosis (h)	Time From Diagnosis to Intervention (h)	Thrombectomy Devices	mTICI	Complication	Antithrombotic Treatment	PedNIHSS Before Procedure	PedNIHSS After 12 -24 h	PedNIHSS After 7 d	ASPECTS (pre/post)	mRS (3 mo)	PSOM (3 mo)
Center 1: Muenster															
7	M	M2	Complex cardiac anomaly	1.5	0.5	Stent retriever: Preset 4×20 mm, sheath: 5F Microcatheter: 2.4F	2b	Spasms, resolved after administration of nimodipine	Preexisting warfarin, peri-interventional Clexane	33	10	9	10/8	2	3
7	F	Carotid-T	Complex cardiac anomality	2	1	Stent retriever: Preset 4×20 mm, sheath: 5F Microcatheter: 2.4F	3	None	Preexisting Warfarin, peri-interventional Clexane	35	8	5	8/8	2	2
14	M	Carotid-T	FCAi	3 (started with fluctuating symptoms 12 h earlier)	1	Stent retriever: Preset 4×20 mm, sheath: 5F Microcatheter: 2.4F	3	Spasms, resolved after administration of nimodipine	Clexane after thrombectomy	5	0	0	9/9	0	0
15	F	M1	FCAi	1.5	0.5	Stent retriever: Preset 4×20 mm, sheath: 8F Microcatheter: 2.8F	2b	None	Clexane after thrombectomy	20	5	5	8/7	1	2
15	F	M1	Complex cardiac anomality	2	0.5	Stent retriever: Preset 4×20 mm, sheath: 6F Microcatheter: 2.4F	3	None	Preexisting warfarin, peri-interventional Clexane	22	7	4	8/8	1	1
Center 2: Hamburg															
10	F	M1	Complex cardiac anomality	0.5	0.5	Stent retriever: Solitaire 4×20 mm, sheath: 5F+5F aspiration catheter Microcatheter: 2.4F	2b	None	Preexisting warfarin, peri-interventional Clexane	8	1	1	7/7	0	0
16	M	M1	Fibromuscular dysplasia	3	0.5	Stent retriever: Solitaire 4×20 mm, sheath: 5F+5F aspiration catheter Microcatheter: 2.4F	3	None	None	3	1	1	8/8	0	0
16	F	M1	Secondary vasculitis after meningitis	1	1	Stent retriever: Solitaire 4×20 mm, sheath: 5F+5F aspiration catheter Microcatheter: 2.4F	2b	None	None	13	10	10	6/6	2	3
17	F	M1	Sepsis-associated coagulopathy	0.5	0.5	Stent retriever: Solitaire 4×20 mm, sheath: 5F+5F aspiration catheter. Microcatheter: 2.4F	3	None	Clexane after thrombectomy	14	3	3	8/8	0	0

Continued

Table 2. Continued

Age, y	Sex (M/F)	Thrombus Location	Etiology	Time From Onset of Symptoms to Diagnosis (h)	Time From Diagnosis to Intervention (h)	Thrombectomy Devices	mTICI	Complication	Antithrombotic Treatment	PedNIHSS Before Procedure	PedNIHSS After 12 -24 h	PedNIHSS After 7 d	ASPECTS (pre/post)	mRS (3 mo)	PSOM (3 mo)
17	M	M1	Thalassemia	1.5	0.5	Stent retriever: Solitaire 4×20 mm, sheath: 5F+5F aspiration catheter. Microcatheter: 2.4F	2b	None	Clexane after thrombectomy	8	1	1	6/6	0	0
Center 3 Lübeck															
5	M	M1	Complex cardiac anomaly	1.5	0.5	Stent retriever: Trevo 4×20 mm, sheath: 5F+5F aspiration catheter Microcatheter: 2.4F	2b	None	Preexisting warfarin, peri-interventional Clexane	10	5	15	10/2 (secondary event right MCA)	3	5
10	M	M1	Dissection	1.5	0.5	Stent retriever: Trevo 4×20 mm, sheath: 5F+5F aspiration catheter Microcatheter: 2.4F	3	None	Clexane after thrombectomy	12	3	3	7/7	1	1

ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; FCAi, focal cerebral arteriopathy of inflammatory subtype; carotid T, internal carotid artery; MCA, middle cerebral artery; mRS, modified Rankin Scale; mTICI, modified Treatment in Cerebral Infarction Score; PedNIHSS, Pediatric National Institutes of Health Stroke Scale; pre, on admission; post, 12-24 hours after admission; PSOM, pediatric stroke outcome measure.

Two recent studies report recanalization treatments in pediatric populations for acute ischemic stroke. Yet in both studies the majority of patients were treated with intravenous thrombolysis, reducing the number of children treated with mechanical thrombectomy to 2[7] and 6 patients.[5] Moreover, of the 11 pediatric patients who underwent endovascular treatment in the recent study by Bigi et al, 5 were treated with intraarterial thrombolysis only. This can be explained by the extended recruitment period of 10 years by Bigi et al.[5] In today's clinical practice, intraarterial lysis as sole treatment is considered inferior to mechanical thrombectomy.[9] In our study we limited the recruitment to 5 years, the time period when stent retrievers have become widely available and have been proven to be the treatment of choice for acute stroke recanalization. Additionally, in our patient collective no patients received additive intravenous thrombolysis. This approach also confines the treatment success to mechanical recanalization, without a bias caused by additive intravenous lysis.

In line with previous reports,[5,6,8] the majority of patients in this study showed good outcomes angiographically, and, most importantly, substantial neurological improvements after the invasive recanalization were observed with a modified Rankin Scale $\leq$2 in 92% (11/12). Currently, there is no robust evidence for intravenous thrombolysis in childhood stroke because existing publications are limited to very small numbers and there has been a publication bias toward short treatment intervals from symptom onset and favorable outcomes in the literature.[10] The Thrombolysis in Pediatric Stroke trial had to be stopped as the majority of pediatric patients did not meet the inclusion criteria, meaning they either presented with mild clinical symptoms only, contraindications to thrombolytics, or delayed admission after 4.5 hours.[11]

It has to be emphasized that adequate caution should be applied to performing thrombectomy in childhood stroke, an intervention that has been studied sufficiently only in adult populations. The interventionalist should be especially aware that, in cases with vasculitis, thrombectomy can carry a high risk of vessel injury, dissection, and thrombosis. Although in our study 1 patient with secondary vasculitis after meningitis had a good outcome, we would refrain from performing routine mechanical thrombectomy in patients with known active vasculitis. However, etiologies are often unknown at the time of admission, and therefore, the emergency decision to perform thrombectomy or not frequently must be made without detailed knowledge about the etiology. Although the 2 patients who were retrospectively diagnosed with focal cerebral arteriopathy of the inflammatory subtype had no periprocedural complications, we are reluctant to recommend thrombectomy in these patients.

Median time to treatment was relatively short in our cohort, which may be attributed to the large number of children with cardiac disease who were already hospital patients at time of symptom onset. In addition, median age of the included patients was 14 years in our study, which is relatively high for pediatric patients but comparable to the recent study by Bigi et al.[5] Last, limits on contrast and radiation exposure are even stricter in children than in adults but tend to be overestimated given the potentially great benefits of a successful intervention.[12]

This study reports a small patient cohort and focuses on children who underwent mechanical thrombectomy. Subsequent reports in which children with and without mechanical thrombectomy are compared are warranted to further elucidate the potential of endovascular thrombectomy to improve outcome after acute ischemic stroke.

Conclusion

Our study adds to the growing evidence that mechanical thrombectomy can be effective and safe not only in adults but also in childhood stroke. However, caution has to be applied because etiology in childhood stroke differs substantially from that in acute ischemic stroke in adults, with potentially major impact on procedure success and safety.

Disclosures

None.

References

1. Goldenberg NA, Bernard TJ, Fullerton HJ, Gordon A, deVeber G; International Pediatric Stroke Study Group. Antithrombotic treatments, outcomes, and prognostic factors in acute childhood-onset arterial ischaemic stroke: a multicentre, observational, cohort study. *Lancet Neurol*. 2009;8:1120–1127.
2. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJ, van Walderveen MA, Staals J, Hofmeijer J, van Oostayen JA, Lycklama a Nijeholt GJ, Boiten J, Brouwer PA, Emmer BJ, de Bruijn SF, van Dijk LC, Kappelle LJ, Lo RH, van Dijk EJ, de Vries J, de Kort PL, van Rooij WJ, van den Berg JS, van Hasselt BA, Aerden LA, Dallinga RJ, Visser MC, Bot JC, Vroomen PC, Eshghi O, Schreuder TH, Heijboer RJ, Keizer K, Tielbeek AV, den Hertog HM, Gerrits DG, van den Berg-Vos RM, Karas GB, Steyerberg EW, Flach HZ, Marquering HA, Sprengers ME, Jenniskens SF, Beenen LF, van den Berg R, Koudstaal PJ, van Zwam WH, Roos YB, van der Lugt A, van Oostenbrugge RJ, Majoie CB, Dippel DW; MR CLEAN Investigators. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11–20.
3. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, Roy D, Jovin TG, Willinsky RA, Sapkota BL, Dowlatshahi D, Frei DF, Kamal NR, Montanera WJ, Poppe AY, Ryckborst KJ, Silver FL, Shuaib A, Tampieri D, Williams D, Bang OY, Baxter BW, Burns PA, Choe H, Heo JH, Holmstedt CA, Jankowitz B, Kelly M, Linares G, Mandzia JL, Shankar J, Sohn SI, Swartz RH, Barber PA, Coutts SB, Smith EE, Morrish WF, Weill A, Subramaniam S, Mitha AP, Wong JH, Lowerison MW, Sajobi TT, Hill MD; ESCAPE Trial Investigators. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015;372:1019–1030.
4. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, San Roman L, Serena J, Abilleira S, Ribo M, Millan M, Urra X, Cardona P, Lopez-Cancio E, Tomasello A, Castano C, Blasco J, Aja L, Dorado L, Quesada H, Rubiera M, Hernandez-Perez M, Goyal M, Demchuk AM, von Kummer R, Gallofre M, Davalos A; REVASCAT Trial Investigators. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372:2296–2306.
5. Bigi S, Dulcey A, Gralla J, Bernasconi C, Melliger A, Datta AN, Arnold M, Kaesmacher J, Fluss J, Hackenberg A, Maier O, Weber J, Poloni C, Fischer U, Steinlin M. Feasibility, safety and outcome of recanalisation treatment in childhood stroke. *Ann Neurol*. 2018;83:1125–1132.
6. Ellis MJ, Amlie-Lefond C, Orbach DB. Endovascular therapy in children with acute ischemic stroke: review and recommendations. *Neurology*. 2012;79:S158–S164.
7. Tabone L, Mediamolle N, Bellesme C, Lesage F, Grevent D, Ozanne A, Naggara O, Husson B, Desguerre I, Lamy C, Denier C, Kossorotoff M. Regional pediatric acute stroke protocol: initial experience during 3 years and 13 recanalization treatments in children. *Stroke*. 2017;48:2278–2281.
8. Cappellari M, Moretto G, Grazioli A, Ricciardi GK, Bovi P, Ciceri EFM. Primary versus secondary mechanical thrombectomy for anterior circulation stroke in children: an update. *J Neuroradiol*. 2018;45:102–107.
9. Haverkamp C, Ganslandt T, Horki P, Boeker M, Dorfler A, Schwab S, Berkefeld J, Pfeilschifter W, Niesen WD, Egger K, Kaps M, Brockmann MA, Neumaier-Probst E, Szabo K, Skalej M, Bien S, Best C, Prokosch HU, Urbach H. Regional differences in thrombectomy rates: secondary use of billing codes in the MIRACUM (Medical Informatics for Research and Care in University Medicine) Consortium. *Clin Neuroradiol*. 2018;28:225–234.
10. Amlie-Lefond C, deVeber G, Chan AK, Benedict S, Bernard T, Carpenter J, Dowling MM, Fullerton H, Hovinga C, Kirton A, Lo W, Zamel K, Ichord R; International Pediatric Stroke Study. Use of alteplase in childhood arterial ischaemic stroke: a multicentre, observational, cohort study. *Lancet Neurol*. 2009;8:530–536.
11. Rivkin MJ, deVeber G, Ichord RN, Kirton A, Chan AK, Hovinga CA, Gill JC, Szabo A, Hill MD, Scholz K, Amlie-Lefond C. Thrombolysis in pediatric stroke study. *Stroke*. 2015;46:880–885.
12. Brenner DJ, Hall EJ. Computed tomography–an increasing source of radiation exposure. *N Engl J Med*. 2007;357:2277–2284.