Beumer et al. Neurovascular Imaging (2016) 2:11
DOI 10.1186/s40809-016-0022-5

Neurovascular Imaging

RESEARCH ARTICLE Open Access

Occurrence of intracranial large vessel occlusion in consecutive, non-referred patients with acute ischemic stroke

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Abstract

Background: The relative frequency of acute intracranial large vessel occlusion (LVO) in patients with acute ischemic stroke (AIS) who could be candidate for intra-arterial treatment (IAT) is not well known. In this study, we determined clinical variables associated with LVO and the proportion of patients with LVO among patients presenting with AIS within 6 h of symptom onset.

Methods: Data of consecutive patients with AIS presenting at the emergency department (ED) of the Erasmus University Medical Center, in the Netherlands, was used. Referrals from other hospitals were excluded.

Results: From 2006 January 1st to 2012 April 30th, 1063 non-referred patients presented at our ED with AIS. 445 (42 %) arrived within 6 h of onset of symptoms. Computed tomography angiography was not performed or was of insufficient quality in 50 patients (11 %) and performed late (≥1 day) in 57 patients (13 %). The remaining 338 with AIS were included in the final analysis. 106 patients (31 %) had LVO, mostly in the anterior circulation (72 %). National Institutes of Health Stroke Scale score was the only variable associated with the presence of LVO (adjusted OR 1.23 per point [95 % Confidence interval: 1.17–1.29]).

Conclusion: Of all patients with acute ischemic stroke who arrive within 6 h of symptom onset at the emergency department, almost one out of three have a intracranial large vessel occlusion and may be candidate for intra-arterial treatment.

Keywords: Large vessel occlusion, Acute ischemic stroke, Thrombectomy candidates, Endovascular procedures, Intra-arterial treatment

Abbreviations: A1, Proximal anterior cerebral artery; AF, Atrial fibrillation; AIS, Acute ischemic stroke; aOR, Adjusted odds ratio; BA, Basilar artery; CI, Confidence interval; ED, Emergency department; ICA, Intracranial internal carotid artery; IAT, Intra-arterial treatment; IVA, Intracranial vertebral artery; IVT, Intravenous alteplase treatment; LVO, Large vessel occlusion; M1, Proximal middle cerebral artery; M2, Distal middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; P1, Proximal posterior cerebral artery; P2, Distal posterior cerebral artery

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Background

Recently published randomized clinical trials showed that intra-arterial treatment (IAT) with retrievable stents for acute ischemic stroke (AIS) was safe and effective in patients with acute intracranial large vessel occlusion (LVO) if they were treated within 6 h of symptom onset [1–6]. Updated guidelines indicate that IAT is now standard of care for AIS patients with LVO [7, 8]. This has great impact on stroke care providers, as the number of performed procedures increases rapidly and resources are limited. To estimate the number of candidates for IAT, it is important to know how many patients with AIS present with LVO.

Observational studies report that 10–61 % of the patients who present at the emergency department (ED) with presumed AIS have LVO. However, these studies did not include unselected, consecutive patients [9], did not use appropriate neuro-imaging in all patients [10], included patients who were transferred from other hospitals [11, 12], or used a restricted time window [13].

Knowledge of the occurrence of LVO is important clinically, for manpower planning and for resource allocation. In this study we describe the occurrence of LVO cases in a consecutive population of all AIS patients admitted to emergency department (ED) within 6 h after onset of symptoms. Moreover, we evaluate clinical predictors of LVO.

Methods

Patients

This retrospective single center study of a consecutive patient cohort was executed by the Erasmus University Medical Center, Rotterdam, the Netherlands. The patient population represents an urban population in a large city, where stroke patients are referred from general practitioners and other centers. Patients with AIS were identified from our Erasmus Stroke Registry, which is operational since 1990. All patients admitted to the ED with a presumed diagnosis of acute stroke are seen by a neurologist or a resident in neurology as part of clinical routine. Patients with AIS were entered into the registry after review and confirmation of the diagnosis by a vascular neurologist. For the present study electronical medical charts and imaging were used. No additional data collection was performed and institutional review board was not needed. All non-referral patients with AIS in the period of From 2006 January 1st to 2012 April 30th who were admitted to the ED were included. Patients had to be 18 years or older. Patients arriving later than 6 h after onset of symptoms at the emergency department were excluded. Patients who did not receive a Computed Tomography Angiography (CTA) or in whom the CTA was of insufficient quality, and patients in whom a CTA was made more than 24 h after intravenous alteplase treatment (IVT) or more than 48 h after stroke onset were also excluded from the present study. Magnetic resonance imaging was never used instead of CTA.

Clinical variables

We determined the clinical location of the occlusion by categorizing symptoms, described by the attending neurologist or resident in neurology in the medical chart, as belonging to occlusion in the territory of the right or left carotid artery or the vertebrobasilar arteries. Furthermore, the National Institutes of Health Stroke Scale (NIHSS) on admission and time from onset of symptoms to arrival at the ED were assessed. Data on medical history were collected from medical records of the patients. The diagnosis of atrial fibrillation (AF) could be based on pre-existing AF, identified through medical history and *de novo* AF during hospitalization. All patients were monitored during the first 24 h after AIS and the diagnosis of *de novo* AF was confirmed by 12-lead ECG. The diagnosis of previous stroke was based on history, transient ischemic attack was not included.

CTA acquisition and analysis

CTA was performed with a 16-slice multidetector CT (MDCT) scanner (Siemens, Sensation 16, Erlangen, Germany), a 64-slice MDCT scanner (Siemens, Sensation 64, Erlangen, Germany) or a 128 slice MDCT scanner (Siemens, Definition AS, Erlangen, Germany) with a standardized optimized contrast-enhanced protocol (100–120 kVp, collimation 16×0.75 mm, 64×0.6 mm, or 128×0.6 mm, pitch ≤1) [14, 15]. The CTA scan ranged from the ascending aorta to the intracranial circulation. Contrast material was given in a bolus of 80 ml (Iodixanol 320 mg/ml, Visipaque, Amersham Health, Little Chalfont, UK), followed by a 40 ml saline bolus chaser. The injection rate was 4 ml/s for both Iodixanol and saline. At the level of the ascending aorta contrast material passage was detected by real time bolus tracking followed by data acquisition. The images were reconstructed by a 100 mm field of view, matrix size 512×512 (real in-plane resolution 0.6x0.6 mm), slice thickness ≤1.0 mm, increment ≤0.6 mm and with an intermediate reconstruction algorithm.

CTA images were sent to a stand-alone workstation (Leonardo, Siemens Medical Solutions, Forchheim, Germany) with dedicated 3D analysis software, and were assessed by experts (GS, PH, AL) who had no clinical information other than a clinical diagnosis of AIS. Of all CTAs the extracranial and intracranial circulation were evaluated blinded without knowledge of the clinical data with multiplanar reformatting software, which allows also reconstruction of sagittal, coronal, and oblique maximum intensity projections from axial sections.

The location of LVO was categorized as: intracranial internal carotid artery (ICA), anterior cerebral artery (A1 segment), proximal middle cerebral artery (M1 segment), distal middle cerebral artery (M2 segment), intracranial vertebral artery (IVA), basilar artery (BA), proximal posterior cerebral artery (P1 segment), distal posterior cerebral artery (P2 segment). Patients suffering from occlusions in multiple segments were categorized by their most proximal intracranial occlusion at the level of the circle of Willis. In addition, occlusions in the extracranial carotid artery and vertebral artery were assessed.

Outcome

LVO was defined as an occlusion in one of the intracranial arteries (ICA, A1, M1, M2, IVA, BA, P1 and P2), accompanied by clinical symptoms that could be attributed to ischemia in the territory of the occluded artery.

Statistical analysis

We used cross tabulation, univariable and multivariable logistic regression analysis. We expressed associations as odds ratios with 95 % confidence intervals (CIs). Statistical analyses were performed with Stata/SE 14.1 (StataCorp. Texas. USA). We considered NIHSS, previous ischemic stroke and AF as possible predictors of occlusion, and we adjusted for age, gender and time to ED.

Results

Over a 6-year period 1063 patients with AIS were admitted to our ED. Of these 1063 patients, 618 (53 %) were excluded because they arrived more than 6 h after onset of symptoms at the emergency department (Fig. 1).

Of the 445 patients who presented within 6 h after onset of symptoms CTA was not performed or of insufficient quality in 50 patients (11 %), and CTA was performed ≥ 24 h after IVT or ≥48 h after stroke onset in 57 patients (13 %) (Fig. 1). Most of these 107 patients with no or late CTA were admitted in the early phase after implementation of acute CTA in AIS patients (2006–2008). Clinical characteristics, including NIHSS at baseline in these 107 patients (median = 5; IQR:2–12) were similar to the total 338 patients (median = 5; IQR:2–11) with CTA in the acute phase ($p = 0.67$). Of the remaining 338 patients with clinical symptoms of AIS, 106 patients (31 %) had LVO. These patients had a mean age of 64 ± 15 years and 53 patients (50 %) were male (Table 1). The median NIHSS on admission was 13 (6–18). Of these, 77 patients (73 %) had an occlusion in the anterior circulation and 29 patients (27 %) had an occlusion in the posterior circulation (Table 2).

Clinical predictors of LVO

Only admission NIHSS was associated with LVO (adjusted Odds Ratio (aOR) = 1.23 per NIHSS point increase [95 % CI: 1.17–1.29]) (Table 1). Patients with NIHSS of 1 or 2 had a 10 % likelihood of LVO (Fig. 2). A score of exactly 12 points on NIHSS indicates a likelihood of 50 % for LVO. When NIHSS ≥ 12, likelihood of LVO is 75 %. NIHSS of 7 and above corresponds with a > 50 % likelihood of LVO. When NIHSS ≥ 20, 21 (91 %) of 23 patients had LVO. Of the two patients with NIHSS ≥ 20 without LVO, one had had a previous stroke, with consequently a pre-stroke modified Rankin Scale score of 3 with a spastic hemiparesis; new stroke symptoms

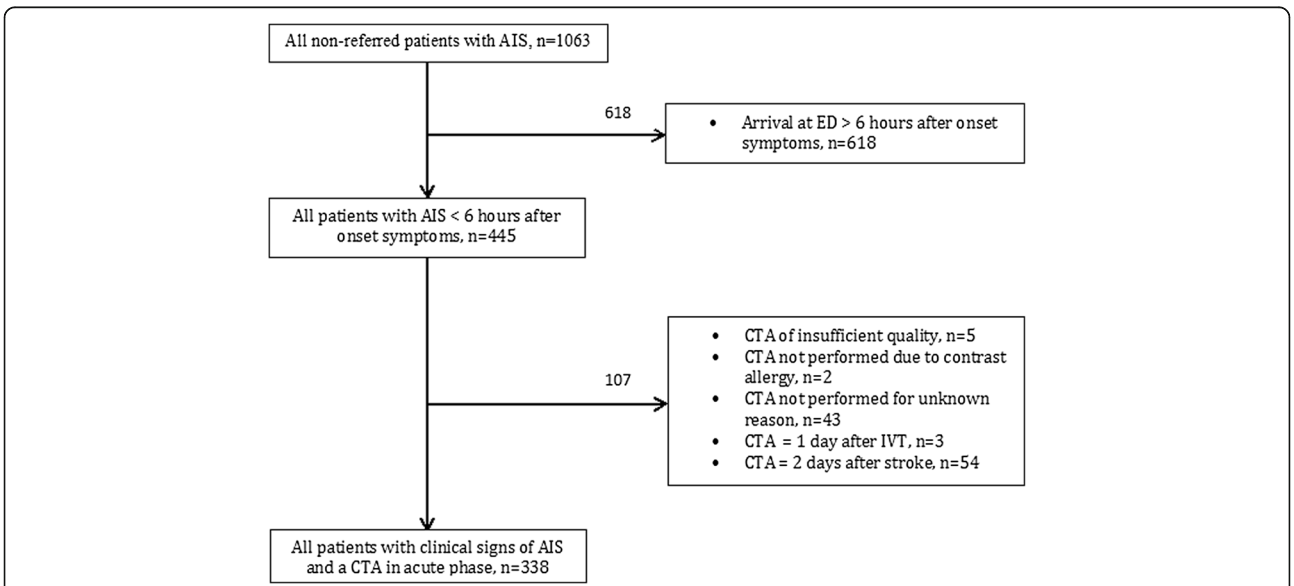

Fig. 1 Inclusion chart of the patients. ED = emergency department, CTA = computer tomography angiography, AIS = acute ischemic stroke

Table 1 Baseline characteristics of the study population with and without acute intracranial large vessel occlusion (LVO)

	LVO (*n* = 106)	No LVO (*n* = 232)	*P*-value
Age (years), mean (SD)	64 (15)	62 (16)	0.26
Male sex, *n* (%)	53 (50 %)	116 (50 %)	1.00
Caucasian ethnicity, *n* (%)	81 (76 %)	184 (79 %)	0.55
Systolic blood pressure, mean (SD)	161 (38)	167 (33)	0.16
Diastolic blood pressure, mean (SD)	85 (21)	89 (19)	0.11
BMI (kg/m^2), mean (SD)	28 (3.8)	27 (5.1)	0.50
Glucose (mmol/L), mean (SD)	7.6 (2.4)	7.3 (2.8)	0.33
Previous ischemic stroke, *n* (%)	18 (17 %)	52 (23 %)	0.22
Previous heart disease, *n* (%)	14 (13 %)	41 (18 %)	0.28
Atrial fibrillation, *n* (%)	14 (13 %)	19 (8 %)	0.16
NIHSS on admission, median (IQR)	13 (6-18)	3 (2–7)	<0.01

All patients arrived at the emergency department within 6 h after onset of symptoms and received a CT-angiography of the intracranial circle of Willis in the acute phase. NIHSS on admission significantly differed between both groups

BMI body mass index, *NIHSS* National Institutes of Health Stroke Scale. NIHSS on admission significantly differed between both groups

were aphasia and facial palsy. The other patient who had a NIHSS score of 22, experienced rapid recovery without IVT. No association was found between the presence of LVO and AF (aOR = 1.10 [95 % CI: 0.43–2.79]) or previous ischemic stroke (aOR = 0.69 [95 % CI: 0.34–1.44]) (Table 1).

Table 2 Distribution and location of acute intracranial large vessel occlusion (LVO)

Anatomical location LVO	Number and percentage of total LVO (*n* = 106)
Anterior circulation (*n* = 77)	
Anterior cerebral artery, A1 segment, *n* (%)	0
Intracranial carotid artery, *n* (%)	23 (22 %)
Middle cerebral artery, M1 segment, *n* (%)	38 (36 %)
Middle cerebral artery, M2 segment, *n* (%)	16 (15 %)
Posterior circulation (*n* = 29)	
Intracranial vertebral artery, *n* (%)	9 (9 %)
Posterior cerebral artery, P1 segment, *n* (%)	8 (8 %)
Posterior cerebral artery, P2 segment, *n* (%)	3 (2 %)
Basilar artery, *n* (%)	9 (9 %)

A1 first segment of anterior cerebral artery, *M1* first segment of middle cerebral artery, *M2* second segment of middle cerebral artery, *P1* first segment of posterior cerebral artery, *P2* second segment of the posterior cerebral artery

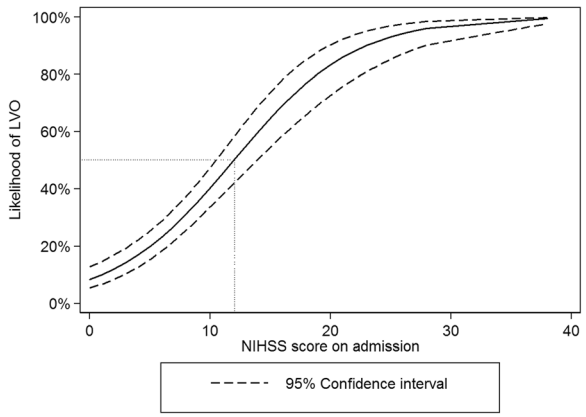

Fig. 2 The association between National Institutes of Health Stroke Scale (NIHSS) and the likelihood of the presence of acute intracranial large vessel occlusion (LVO) confirmed by CTA, in 338 patients with acute ischemic stroke, admitted within 6 h of symptom onset. For each point increase in NIHSS, aOR is 1.23 (95 % CI: 1.17-1.29) for having LVO. At NIHSS 12 the chance of having LVO is 0.5 (50 %)

Discussion

This study of an unselected non-referred consecutive cohort of AIS patients arriving at the ED within 6 h of symptom onset, showed that almost one out of three have LVO and may be IAT candidate.

Clinical practice

Our study suggests that almost one third of all patients with AIS may be candidates for IAT, since they had LVO in the proximal anterior or posterior circulation and these LVO locations are currently treated in clinical practice in the Netherlands and registered in the MR CLEAN Registry (www.mrclean-trial.org). This is in concordance with data from Copenhagen where 29 % had LVO. The population in the latter study was different from ours, since only IVT candidates were studied, which implies a restricted time window and extra criteria for candidates in comparison to IAT candidates [13]. However, both these estimates are based on a consecutive AIS population presenting at EDs. In two large and well documented studies from Bern, using an overlapping population, 40–61 % of patients had LVO [12]. However, these studies included patients who were referred from other centers, which implies selection and at least partly explains the higher proportion of patients with LVO. This makes it difficult to extrapolate these estimates to other settings.

Our results confirm that NIHSS score at baseline is the most important predictor of LVO, as reported previously [12, 13, 16]. We found that a vast majority (91 %) of patients with NIHSS ≥ 20 had LVO. This high percentage of occlusion in patients with severe clinical

symptoms is in concordance with other studies, where more than 95 % of patients with NIHSS ≥ 20 had an occlusion [12, 13]. However, our study also emphasizes that patients with low NIHSS could have LVO.

Limitations

Several limitations may influence the generalizability of our study results. First, our study was a single center study in an academic hospital. However, our center is a centrally located comprehensive stroke center and it has no restrictions on access to the ED. We present a consecutive series of non-referred patients, which we believe is representative for any urban population in a large city like Rotterdam. Second, 107 patients (24 %) who presented at the ED within 6 h after symptom onset did not get a CTA in the acute phase. Most of these patients were admitted to our hospital in the first years after implementation of acute CTA in AIS patients, in 2006. In that early period CTA was sometimes performed later or not at all, despite being part of standard protocol. Most importantly there was no selection bias based on stroke severity as there was no difference in baseline NIHSS between the patients with and without CTA. Since NIHSS at baseline is the most important predictor of LVO, there is no reason to assume that the rate of LVO in these patients differs from in those who had CTA in the acute phase and were included in our analysis.

Conclusion

Of all patients with acute ischemic stroke who arrive within 6 h of symptom onset at the emergency department, almost one out of three will have an intracranial large vessel occlusion and may be eligible for intra-arterial treatment.

Acknowledgements

None.

Funding

None.

Availability of data and materials

Data is not available publicly as this is a single center study where individual privacy could easily be compromised. For access to a minimal dataset the authors should be contacted.

Authors' contributions

DB & MM contributed equally to this paper: literature search, figures, study design, data analysis, data interpretation, writing. GS: data collection, data analysis & writing of first draft. SF & PH: data analysis & writing. RVO & WZ: study conception & critical review of the manuscript. DD & AL: study conception, data analysis & critical review of the manuscript. All authors read and approved the final manuscript.

Competing interests

DD was PI of the MR CLEAN trial, which was partly funded by the Dutch Heart Foundation and by unrestricted grants from AngioCare BV, Medtronic/Covidien/EV3®, MEDAC Gmbh/LAMEPRO, Penumbra Inc., Stryker®, and Top Medical/Concentric.

Erasmus MC received funds from Stryker® and Bracco Imaging® for consultations by DD.

MUMC received funds from Stryker® and dePuySynthes® for consultations by WZ.

Consent for publication

N.A.

Ethics approval and consent to participate

For the present study electronical medical charts and imaging were used. No additional data collection was performed and institutional review board was not needed.

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Received: 9 August 2016 Accepted: 29 August 2016
Published online: 05 September 2016

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