

Time to computerized tomography scan, age and mortality in acute stroke

Short title: Time to CT, age and mortality in acute stroke

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Abstract

Background: Time to computerized tomography (CT) is important to institute appropriate and timely hyper-acute management in stroke. We aimed to evaluate mortality outcomes in relation to age and time to CT scan.

Methods: We used routinely collected data in eight National Health Service Trusts in East of England between September 2008 and April 2011. Stroke cases were prospectively identified and confirmed. Odds ratios for unadjusted and adjusted models for age categories (<65, 65–74, 75–84 and ≥85 years) as well as time to CT categories (<90 minutes, ≥90 to <180 minutes, ≥180 minutes to 24 hours and >24 hours) and the in-hospital and early (<7 days) mortality outcomes were calculated.

Results: Of 7,693 patients (mean age 76.1 years, 50% male) included, 1,151 (16%) died as inpatient and 336 (4%) died within seven days. Older patients and those admitted from care home had a significantly longer time from admission until CT ($p < 0.001$). Patients who had earlier CT scans were admitted to stroke units more frequently ($p < 0.001$) but had higher in-patient ($p < 0.001$) and seven-day mortality ($p < 0.001$). Whilst older age was associated with increased odds of mortality outcomes, longer time to CT was associated with significantly reduced within 7 day mortality (corresponding ORs for above time periods were 1.00, 0.61 (0.39–0.95), 0.39 (0.24–0.64) and 0.16 (0.08–0.33) and in-hospital mortality (ORs 1.00, 0.86 (0.64–1.15), 0.57 (0.42–0.78) and 0.71 (0.52–0.98)).

Conclusions: Older age was associated with a significantly longer time to CT. However, using CT scan time as a benchmarking tool in stroke may have inherent limitations and it does not appear to be a suitable quality marker.

Keywords: Stroke; Age; Computerized tomography; Outcome; Mortality

List of abbreviations

AS&HCN	Anglia Stroke & Heart Clinical Network
ASCNES	Anglia Stroke Clinical Network Evaluation Study
CT	Computerised tomography
LACS	Lacunar stroke
mRS	Modified Rankin Score
NHS	National Health Service
NIHR	National Institute of Health Research
NIHSS	National Institute of Health Stroke Score
OCSP	Oxfordshire Community Stroke Project
PACS	Partial anterior circulation stroke
POCS	Posterior circulation stroke
SHA	Strategic Health Authority
TACS	Total anterior circulation stroke
TIA	Transient ischemic attack
tPA	Tissue plasminogen activator
UK	United Kingdom
USA	United States of America

Introduction

Treatment of acute stroke is aimed at salvaging potentially viable brain. Intravenous tissue plasminogen activator (tPA) is recommended if appropriate¹ as it is associated with reduced infarct size and better functional outcomes if this is achieved rapidly.² The delivery of therapy within recommended timeframe relies on rapid computerized tomography (CT) imaging to exclude hemorrhage, demonstration of which is also important as this may identify such patients for appropriate management.² Hence, delays in CT scanning in acute stroke may have adverse impact on the patient.

While age is a major determinant of mortality outcome in any acute illness, it may also be an important determinant of the stroke care they receive in acute settings, with sub-optimal compliance with many evidence-based processes of care for older stroke patients compared to younger patients, including receiving CT scans.³ Discrimination against older people and problems with overt and covert rationing of health care against older people has been previously highlighted.⁴ Not surprisingly, ageism against older patients has been the topic of much debate in various aspects including stroke management.

We have previously shown that increase in CT scan rate in older age was associated with a lower inpatient case-fatality rate, reduced length of acute hospital stay and more favourable discharge destination for older people with stroke compared with their younger counterparts.⁵ However, the study almost pre-dated the introduction of thrombolysis for ischemic stroke in the UK. Whether time to CT imaging is associated with a better outcome in stroke in the context of age in a consecutive stroke patient population has not been examined.

There is a need for further research aimed at developing an understanding of why age-related differences exist in stroke management, particularly whether age differences in CT scan times exists and if so what were the impacts on acute mortality outcome. We aimed to

better understand the complex relationships between age of the patient, time to CT (decision based on perceived clinical needs and service factors) and the acute stroke outcomes. We therefore investigated whether age is a determinant of the time period from arrival to hospital to CT scan and also examined the effect of age and time to CT scan on in-patient and early (within 7- day) mortality in acute stroke controlling for potential confounders.

Materials and methods

The Anglia Stroke & Heart Clinical Network (AS&HCN) was established by the East of England Strategic Health Authority (SHA) to support the development of stroke services in three counties in the East of England from which participants in Anglia Stroke Clinical Network Evaluation Study (ASCNES) was drawn.⁶ The ASCNES was funded by the NIHR Research for Patient Benefit Programme (PB-PG-1208-18240) and obtained ethical approval from the Norfolk Research Ethics Committee. The AS&HCN was funded by the NHS Improvement Programme through the East of England SHA. AS&HCN data were linked to ASCNES as part of collaboration agreement as per requirement for ASCNES anonymized data sharing.

Patients recorded in the AS&HCN registry were those admitted between September 2008 and April 2011 to eight acute NHS Trusts in the East of England region with the catchment population of approximately 2.5 million. All patients included in the study were confirmed stroke cases (either ischemic or hemorrhagic stroke). Transient ischemic attacks and other vascular causes of neurological deficits presenting with stroke symptoms (e.g. (TIA) subdural hematoma, subarachnoid hemorrhage) were excluded from this study. AS&HCN data collection was aimed at gathering process of care data of stroke services in relation to National targets and guidance from the Royal College of Physicians.⁷

The variables used in the current study were participants' age, sex, pre-stroke residence status (categorical - home, care home, other (e.g. rehabilitation facilities, sheltered accommodation)), pre-stroke modified Rankin (prestroke mRS), date of admission, time of admission, date of CT scan, time of CT scan, admission to stroke unit, presence of atrial fibrillation, type of stroke (ischemic or hemorrhagic), Oxfordshire Community Stroke Project (OCSP) classification (lacunar stroke (LACS), partial anterior circulation stroke (PACS), total anterior circulation stroke (TACS) and posterior circulation stroke (POCS)),⁸ systolic blood pressure, intravenous thrombolysis status, in-patient mortality and discharge destination. Those with diagnosis of TIA, missing time to CT scan and missing discharge destination were excluded (n=1,063) (see Supplementary Figure 1).

Statistical analyses were performed using Stata software, version 12.1 MP (Stata Corporation, Texas, USA). Medians, percentages, odds ratios (OR) and their 95% confidence intervals (CI) are reported as appropriate. The characteristics of patients and outcomes defined as in-patient death and in-patient death within 7 days according to time to CT scan were presented descriptively. Time to CT scan was calculated by subtracting time of CT scan by time of arrival to hospital. The time to CT categories were defined as <90 minutes, 90-180 minutes, >180 minutes to 24 hours and >24 hours based on nearest quartile cut off points.

The odds ratios (95% CI) for unadjusted and adjusted models for age categories and the study outcomes, in-patient mortality and within 7-day mortality, were also calculated. Adjusted model 1 adjusted for age and time taken to have CT after admission and model 2 additionally adjusted for sex, pre-stroke mRS, stroke type and OCSP classification. Age categories were defined as less than 65 years, 65 years to 74 years, 75 years to 84 years and ≥ 85 years. The reference category for all outcomes was the bottom category (<65 years and CT time < 90 minutes). A 3D plot of adjusted odds ratios of the 4 age categories and 4 times to CT categories was also constructed to better understand the complex relationships between

CT time (decision to CT early or late) vs. age vs. outcome using less than 65 years old with CT less than 90 minutes as the reference category for the both outcomes examined.

Results

Table 1 provides the sample characteristics and study outcomes according to the time to CT scan. Older patients were associated with a significantly longer time from admission until CT ($P < 0.001$) and had more atrial fibrillation ($P < 0.03$). Patients from care homes had a longer wait from admission until CT ($P < 0.001$). Significantly higher proportion of patients who had CT scans within 90 minutes of admission were thrombolysed compared to those with a longer time from admission until CT ($P < 0.001$). Patients who had total anterior circulation strokes (TACS) did not get CT as urgently as those with posterior circulation strokes (POCS) ($P < 0.001$). Patients who had earlier CT scans were also admitted to stroke units more frequently than those with a longer time from admission until CT ($P < 0.001$) but had higher in-patient and seven-day mortality (P for both outcomes < 0.001).

Table 2 shows the odds ratio and corresponding 95% CI for inpatient and seven-day mortality according to age groups and then according to time to CT scan categories. After adjusting for age and time to CT scan (model 1), patients who were older had greater the odds of dying as an inpatient than younger patients. However those patients who had CT scans after 24 hours had lower odds of dying (OR 0.41 (0.34-0.49)) as an inpatient compared to those who had CT scans within 90 minutes (OR 1.00), but greater odds of dying as an inpatient compared with patients who had a CT scan between 8 and 24 hours (OR 0.36 (0.30-0.43)). Similar findings were observed in model 2 after adjusting for age, time to CT, sex, pre-stroke mRS, stroke type and OCSP classification.

After adjusting for age and time to CT scan (model 1), older patients also had greater odds of dying within seven days compared with younger patients. Those patients who had CT scans after 24 hours had lower odds of dying (OR 0.11 0.07-0.18)) within seven days compared to those who had CT scans within 90 minutes (reference category). After adjusting for age, time to CT, sex, pre-stroke mRS, stroke type and OCSP classification (model 2),

those who had CT scans between 8 and 24 hours had lower odds of dying (OR 0.39 (0.24-0.64) within seven days compared to patients who had CT scans within 90 minutes (reference category), but greater odds of dying within seven days compared with patients who had CT scans after 24 hours (OR 0.16 (0.08-0.33)).

Figure 1 shows the 3D plot of the adjusted odds ratios of age group versus time to CT group for both in-patient mortality (Figure 1A) and seven-day mortality (Figure 1B).

Discussion

In this study we found that older age was associated with a significantly longer time to receiving brain CT imaging and also associated with increased stroke mortality after admission with an acute stroke compared to younger age. Additionally we found that patients admitted from care homes had a longer wait from admission until CT and patients who had total anterior circulation strokes did not get CT imaging as urgently as those with posterior circulation strokes. We also found that patients who had earlier CT scans received IV thrombolysis more often compared to those with a longer time from admission until CT. Moreover we found that patients who had earlier CT scans were admitted to stroke units more frequently than those with a longer time from admission until CT but had higher inpatient and seven-day mortality. This study adds to our previous work by evaluating the impact of CT scan times on in-patient mortality thus provides some insight into the age-related differences in stroke management and outcome in the context of thrombolysis treatment in the UK setting.

Decision to perform an early CT scan appears to be driven by age and frailty indicator depicted by place of residence as well as the severity of stroke and also by potential for intravenous thrombolysis. Therefore those with very mild or most severe forms of strokes who were not suitable to be thrombolysed had CT scans much later. However, irrespective of

this, we have shown that a disproportionately high number of older people wait longer for a CT scan compared to their younger counterparts and this relationship appears to be linear. This was also true for patients arriving from care homes. This is in keeping with a recent systematic review which examined the published literature on whether older acute stroke patients received the same quality of care as younger patients, as measured by compliance with evidence-based process indicators.³ The authors of this review concluded that patients' age may be an important determinant of the stroke care they receive in acute settings, including receiving CT scans, and that there was sub-optimal compliance with many evidence-based processes of care for older stroke patients compared to younger patients.³

Previous studies which have examined the rates of CT scans and investigations in stroke management report similar findings. In a multi-centre European study of 4,499 patients with first-time stroke evaluated with regard to functional outcome patients aged ≥ 80 years were compared with the younger age groups and brain imaging and other diagnostic tests were significantly less used in the older patients.⁹ Moreover a further study investigating variations in the use of diagnostic procedures across multiple European hospitals in first-time stroke patients also found that patients with increasing age were less likely to receive the diagnostic standard.¹⁰ This was also echoed in studies of patients with first-time strokes.^{11,12} The high mortality odds observed in older patients may be attenuated if they had similar timing for CT as their younger counterparts.

We found that patients who had earlier CT scans were admitted to stroke units more frequently than those waiting longer but had higher inpatient and seven-day mortality rates. The latter finding differs from a study examining three month mortality and functional outcome of European patients admitted to hospital with first time strokes.¹³ The authors in this study conclude that CT scan rates were higher in younger patients compared with older patients, and older stroke patients who did not have a CT scan had a significantly increased

mortality rate.¹³ Whilst previous such studies have focused on the rates rather than timing of CT in the management of stroke, our study has examined the rates through different time frames in the context of potential cofounders. We found that people who had early CT scans had higher mortality even controlling for age. This could be because those who had CT scans had more severe strokes, regardless of age.

Our study has several strengths. This study has a large sample size of just under eight thousand patients and includes eight diverse NHS trusts allowing us to capture variation in the case-mix and the outcomes between different stroke services and hence the generalizability in the UK NHS setting. All stroke cases were ascertained based on clinical diagnosis and neuroimaging. The sample consists of wide ranging age bands, prestroke disability and function depicted by broad spectrum of prestroke mRS and residence status, medical factors that contribute to acute mortality outcomes such as blood pressure,^{14,15} atrial fibrillation^{16,17} and treatment with intravenous tPA.^{18,19}

Our study also has limitations. The main limitation was that we had fair amount of missing data for pre-stroke mRS and data on atrial fibrillation. However, the internal relationship between time to CT and stroke outcome is unlikely to be affected by the missing data. If any, truncation of the sample distribution will only reduce the sample size and this is likely to attenuate the associations observed. Aside from atrial fibrillation, the routine AS&HCN data did not capture the other co-morbidities and this might have influenced the time of CT scan and the subsequent management. Nevertheless, we adjusted for pre-stroke mRS which likely to reflect co-morbidities and their impact on physical ability. Some patients with stroke might not have been captured by our study e.g. those which are patients with mild stroke (not admitted to hospital or detected at TIA clinic) and very severe stroke (died before admission or decision was made not to admit to hospital i.e. palliation only). Nevertheless, this is not the remit of the study and stroke admitted to health care facilities are

undoubtedly important. We also did not have data on National Institute of Health Stroke Scale (NIHSS) for majority and hence we were unable to control the NIHSS, which may have been useful. Nevertheless, we used OCSP classification which has prognostic significance and closely linked to NIHSS.^{20,21}

In summary, there are age-related differences in stroke management with regard to CT scan times. The decision to perform CT urgently appears to be dependent on patient's age, stroke severity, pre-stroke disability and residence status and thus overall perceived need of urgent CT by the clinical team. Furthermore, there is no evidence that early CT scan is associated with lower mortality outcomes. However, excess mortality rate associated with older age may be at least partially accounted for by relative delay in CT scanning compared to their younger counterparts. We conclude CT scan time as a benchmarking tool in stroke may have inherent limitations and may not be suitable as a quality marker. This study provides new insight that any benchmarking tools proposed to evaluate stroke services should not be based on factors/variables that can be influenced by clinician's decision making process on need base.

Disclosures: None

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Contributors

PKM is the PI of the ASCNES and conceptualize the study. CSK performed the data analysis. SDM was responsible for data management. JFP, MOB, GMP, AKM, and EAW are co-applicants of the ASCNES. DJD, AKM, AN, PA, KW, RS and JN are site PIs of the eight collaborating NHS Trust. ACK, CSK and PKM wrote the first draft of the manuscript and all of the authors contributed to the manuscript and approved the final manuscript.

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Legends

Figure 1: 3D plot of adjusted odds ratio of age (4 groups) vs. time to CT (4 groups) for in-patient mortality (Figure 1A) and seven-day mortality (Figure 1B)

Table 1: Sample characteristics and study outcomes according to time to CT from admission in Anglia Stroke & Heart Clinical Network

Table 2: Odds ratio for inpatient and 7-day mortality according to age categories and time to CT categories in Anglia Stroke & Heart Clinical Network

Figure 1: 3D plot of adjusted odds ratio of age (4 groups) vs. time to CT (4 groups) for in-patient mortality (Figure 1A) and seven-day mortality (Figure 1B)

Figure 1A

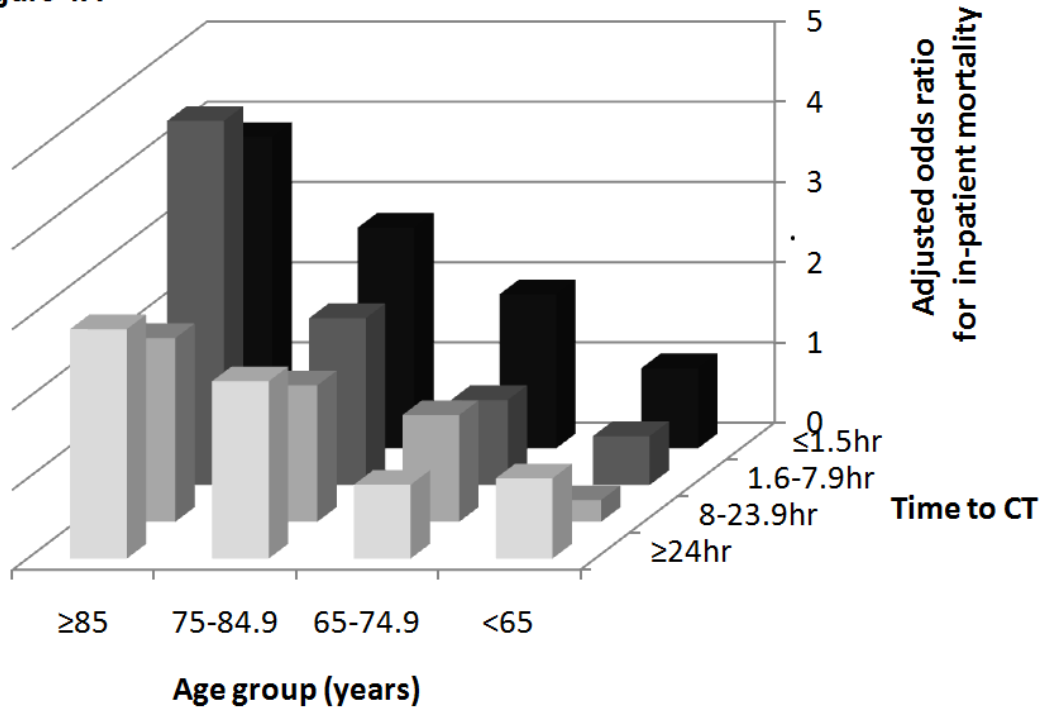


Figure 1B

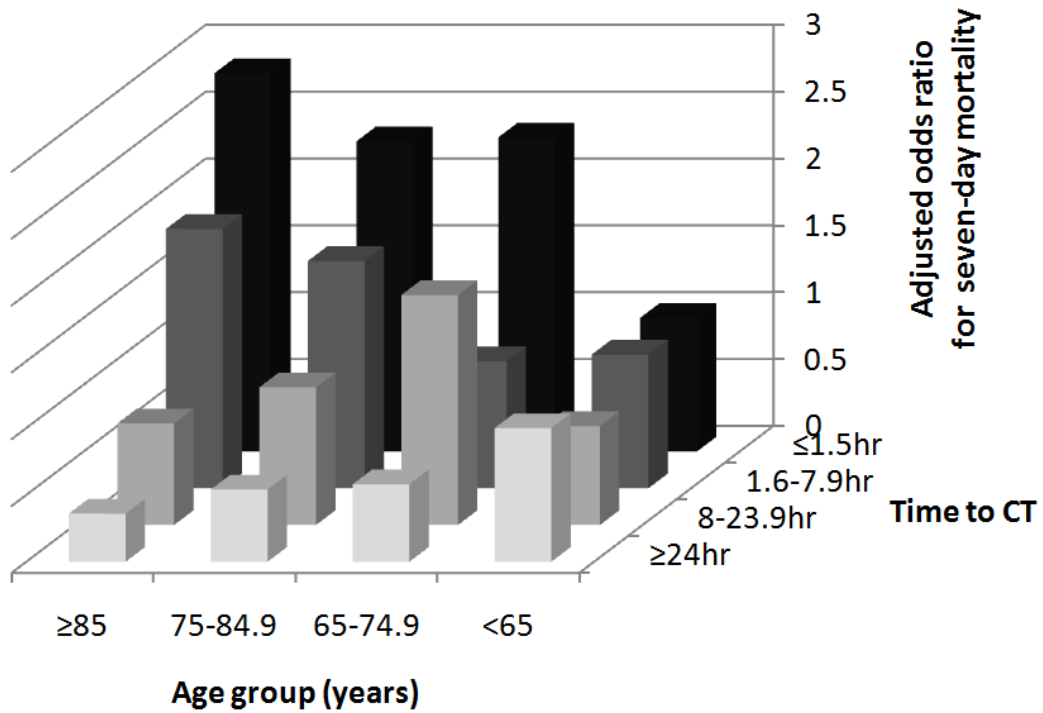


Table 1: Sample characteristics and study outcomes according to time to CT from admission in Anglia Stroke & Heart Clinical Network

Variable	Time to CT					P-value	Total number
	Time 1 <90 min	Time 2 90 min to 8 hrs	Time 3 8 hours to 24 hrs	Time 4 >24 hrs			
N	1,886	2,134	2,019	1,654	-		7,693
Age (years)	73 (\pm 14)	75 (\pm 13)	78 (\pm 12)	79 (\pm 11)	<0.001		7,610
Sex							
Men, n (%)	975 (52%)	1,034 (50%)	958 (49%)	748 (47%)	0.02		7,488
Pre-Stroke Modified Rankin Score							
0	753 (63%)	694 (57%)	638 (51%)	360 (38%)	<0.001		2,445(53%)
1	178 (15%)	197 (16%)	207 (17%)	198 (21%)			780 (17%)
2	117 (10%)	130 (11%)	155 (12%)	135 (14%)			537 (12%)
3	93 (8%)	123 (10%)	141 (11%)	140 (15%)			497 (11%)
4	39 (3%)	62 (5%)	89 (7%)	98 (10%)			288 (6%)
5	18 (2%)	17 (1%)	19 (2%)	25 (3%)			79 (2%)
Total							4626
Place of residence prior to admission							
Home	1,354 (91%)	1,379 (89%)	1,199 (88%)	917 (85%)	<0.001		4,849(88%)
Care home	94 (6%)	108 (7%)	119 (9%)	136 (13%)			457 (8%)
Other	47 (3%)	63 (4%)	52 (4%)	26 (2%)			188 (3%)
Total							5494
Stroke type							
Ischemic	1,474 (82%)	1,713 (86%)	1,707 (92%)	1,304 (90%)	<0.001		6,198(87%)
Hemorrhagic	311 (18%)	272 (14%)	158 (8%)	137 (10%)			898 (13%)
Total							7096
OCSP classification							
TACS	200 (18%)	306 (26%)	374 (31%)	299 (30%)	<0.001		1,179(26%)
PACS	452 (40%)	434 (37%)	512 (41%)	402 (40%)			1,800(39%)
LACS	164 (14%)	203 (17%)	161 (13%)	148 (15%)			676 (15%)

POCS	326 (29%)	237 (20%)	196 (16%)	157 (16%)		916 (20%)
Total						4571
Systolic BP	162 (32%)	159 (31%)	158 (29%)	156 (28%)	<0.001	6,605
Thrombolysis	262 (15%)	19 (1%)	2 (0.1%)	6 (0.4%)	<0.001	289 (45%)
AF	317 (28%)	323 (31%)	209 (26%)	179 (31%)	0.03	1,028(295)
Admitted to stroke unit	504 (80%)	708 (75%)	808 (75%)	682 (70%)	<0.001	2,702(74%)
In-patient mortality	391 (21%)	327 (15%)	218 (11%)	215 (13%)	<0.001	1,151(15%)
In-patient mortality within 7-days	178 (9%)	91 (4%)	42 (2%)	25 (2%)	<0.001	336 (4%)

The numbers presented are mean (SD), and number (%).

Abbreviations: CT=computed tomography, OSCP=Oxfordshire Community Stroke Project, TACS=total anterior circulation stroke, PACS=partial anterior circulation stroke, LACS=lacunar stroke, POCS=posterior circulation stroke.

Table 2: Odds ratio for inpatient and 7-day mortality according to age categories and time to CT categories in Anglia Stroke & Heart Clinical Network

	In-patient mortality				7-day mortality			
	No. death/ No. total	Unadjusted odds ratio (95% CI) [#]	Adjusted odds ratio model 1 (95% CI) ^{*†}	Adjusted odds ratio model 2 (95% CI) ^{*‡}	No. death/ No.total	Unadjusted odds ratio (95% CI) [#]	Adjusted odds ratio model 1 (95% CI) ^{*†}	Adjusted odds ratio model 2 (95% CI) ^{*‡}
Age cat 1	66/1,331	1.00	1.00	1.00	26/1,331	1.00	1.00	1.00
Age cat 2	141/1,483	2.01 (1.49-2.72)	2.17 (1.60-2.94)	1.92 (1.14-3.23)	52/1,483	1.82 (1.13-2.94)	2.10 (1.30-3.40)	2.90 (1.24-6.80)
Age cat 3	412/2,607	3.60 (2.75-4.71)	4.11 (3.13-5.39)	3.15 (1.98-5.01)	136/2,607	2.76 (1.81-4.22)	3.56 (2.32-5.47)	3.03 (1.37-6.70)
Age cat 4	519/2,189	5.96 (4.56-7.77)	7.34 (5.60-9.62)	4.78 (2.99-7.65)	119/2,189	2.98 (1.93-4.58)	4.36 (2.82-6.74)	3.14 (1.39-7.09)
Time to CT 1	391/1,886	1.00	1.00	1.00	178/1,886	1.00	1.00	1.00
Time to CT 2	327/2,134	0.69 (0.59-0.81)	0.59 (0.50-0.70)	0.86 (0.64-1.15)	91/2,134	0.43 (0.33-0.55)	0.39 (0.30-0.50)	0.61 (0.39-0.95)
Time to CT 3	218/2,019	0.46 (0.39-0.55)	0.36 (0.30-0.43)	0.57 (0.42-0.78)	42/2,019	0.20 (0.14-0.29)	0.17 (0.12-0.25)	0.39 (0.24-0.64)
Time to CT 4	215/1,654	0.57 (0.48-0.68)	0.41 (0.34-0.49)	0.71 (0.52-0.98)	25/1,654	0.15 (0.10-0.23)	0.11 (0.07-0.18)	0.16 (0.08-0.33)

Logistic regression model unadjusted, adjusted model 1 (age and time to CT only) *adjusted model 2 (age, time to CT, sex, pre-stroke modified Rankin, stroke type and OCSF classification in model)

Age cat 1=<65, age cat 2= \geq 65 &<75, age cat 3= \geq 75 &<85, age cat 4= \geq 85

Time to CT 1=<90 min, Time to CT 2= \geq 90min &<8 hours, Time to CT 3= \geq 8 hours &<24 hours, Time to CT 4= \geq 24 hours

[#]n=7,693

[†]n=7,610

[‡]n=3,481

Supplementary Figure 1: Flow diagram of reason for exclusion

