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A Real-World Perspective on Interfacility Transfers of Acute Ischemic Stroke from a Semi-Rural Center

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Abstract

Introduction: Interfacility transfers (IFT) of acute ischemic stroke (AIS) may not always lead to a better prognosis. **Methods:** Retrospective cohort study included AIS patients at an emergency department (ED) with telestroke. Multiple linear regression for departure time from ED (DT), quantile regression for length of in-hospital stay (LOS), and Kaplan-Meier estimator with Cox proportional hazards model for one-year survival (SV) were performed. **Results:** 192 patients included were categorised according to IFT. Mechanical thrombectomy was performed in 50% who had been transferred. Differences were found in DT, discharge disposition and LOS. An inverse relationship existed between DT and NIHSS. The strongest predictor of LOS was TACS (β = 3.14 [0.03 - 8.49]; p = 0.005). SV was related to IFT (HR 4.68 [1.37 - 16.07]; p = 0.014), age (HR 1.1 [1.04 - 1.17]), BI < 60 (HR 2.7 [1.02 - 7.1]), TACS (HR 9.82 [1.08 - 88.95]) and NIHSS ≥ 6 (HR 2.85 [1.05 - 7.74]). **Conclusions:** Shared decision-making with a stroke unit through telemedicine enabled a standardised clinical management in a non-metropolitan setting. Several improvement opportunities were identified: multimodal computed tomography availability before transfer, as well as optimization of response time and training in neurosonology of emergency physicians.

Keywords

Stroke, Emergency Room, Transportation of Patients, Prognosis

1. Introduction

Ischemic cerebrovascular disease (iCVD) represents a high-impact process in Spanish healthcare system. In the year 2017, stroke was the main diagnosis of 61,164 among 4,862,352 hospital admissions; 78% aged ≥65 years, a mean length

of in-hospital stay (LOS) of 10.79 days and a mean cost of €6137.64 per admision [1]. In addition, iCVD was responsible for 7643 in-hospital deaths (1.8% of total), 95% aged ≥65 years (59% women) [2]. In the Autonomous Community of Catalonia, reperfusion strategy for acute ischemic stroke (AIS) was indicated in total for 3752 patients, exclusively in accordance with a standardised protocol by the health care administration [3].

An American study that analysed data for 2006-2014 period observed a 300% increase in the probability of interfacility transfer (IFT) from ED, especially in patients from rural settings [4]. Mechanical thrombectomy of AIS involves a network of highly complex centers geostrategically located, often requiring an IFT. Sonig *et al.* [5] described that the hospitalisation costs of those transferred ($97,547) differed from those who were not ($70,325). Consequently, the increase in costs and variability between centres has generated the need to establish efficiency criteria. Therefore and with this objective, the implementation of telematic tools for specialised consultation [6] aims to increase diagnostic accuracy [7] and avoid transfers considered futile because so many times they do not involve the application of additional techniques by the neurologist.

Another common reason for IFT is transient ischemic attack (TIA). Some authors have published statistical models that predict the development of AIS after a short clinical event [8] [9], although additional neuroradiology techniques have been suggested to improve the discriminatory power of these scores [10], such as ultrasound of the supraaortic trunks (SAT) in the first 24 - 48 hours [11].

Therefore, we consider it necessary to explore IFT process of patients with AIS/TIA through a cohort of an unselected population, such as patients attended by emergency physicians in a semi-rural community hospital. The objective of this study was to describe clinical characteristics of patients with AIS/TIA, diagnostic process, and prognostic impact of IFT in order to identify opportunities to improve decision making.

2. Methods

We performed a retrospective cohort study, from January to December of 2017, in ED of Vic University Hospital. Patients consecutively included were aged ≥ 16 years and diagnosed with AIS/TIA. False positives as well as those that lacked evolutive data were excluded. Evolutive follow-up was carried out by accessing shared medical history of the catalan healthcare system. Patients (or caregiver) must give their consent to be included in the study.

Cases were selected by reviewing the administrative record of past episodes coded as AIS or TIA. Medical charts are computerised in our center and hence variables defined in study protocol were recorded directly in an electronic database (Microsoft® Excel). The researchers included all episodes in which an acute neurological deficit was described, with a 24-hour limit for TIA. 35 independent variables were collected: 2 demographic (age and gender), 3 basal functional status and comorbidity scales (Barthel Index < 60 [BI], mRankin ≤ 1, Charlson Index [CI]), 4 cardiovascular risk factors (smoke, hypertension, diabetes melli-

tus, dyslipidemia), 5 comorbidities (cognitive impairment, atrial fibrillation [AF], mitral valvulopathy, peripheral arteriopathy, ischemic cardiopathy), 8 chronic medications (acetylsalicylic acid 100 mg, acetylsalicylic acid 300 mg, P2Y12 inhibitors, vitamin K inhibitors, direct oral anticoagulants, angiotensin II converting enzyme inhibitors, angiotensin II receptor antagonists, lipid-lowering drugs), 13 from the acute episode (type of access to ED [by own means, primary or prehospital or subacute healthcare], Oxfordshire/Bamford topographic diagnosis [LACS, PACS, POCS, TACS], AF + INR < 2 seconds, time of onset of symptoms, wake-up stroke, NIHSS ≥ 6, NIHSS ≥ 6 + mRankin ≤ 1, alteplase [rtPA], TIA SAT, AIS SAT, echocardiography, MRI). Multimodal CT (MCT), mechanical thrombectomy (MT) and admission to a stroke unit (SU) were registered only in transferred patients. Furthermore, 9 follow-up variables: DT from ED, discharge disposition (home, death, subacute healthcare center), ED reconsultation, LOS, 30-day death, 1-year death, 1-year death in NIHSS ≥ 6 + mRankin ≤ 1 group, 1-year delta Barthel Index and mRankin in NIHSS ≥ 6 group.

The study was undertaken following ethical principles for human research of Helsinki Declaration, and the protocol was approved by the Committee of Ethics and Clinical Investigation of Osona Foundation for Health Research and Education (CEIC code 2018978, own code PR209).

Quantitative variables were expressed as mean and standard deviation, if they followed a normal distribution, according to the Kolmogorov-Smirnov test, or median and interquartile range if not. Qualitative variables were described as absolute values and ratios.

The cohort was categorised according to IFT (TRANSFER, NON-TRANSFER). Only TRANSFER was sub-divided depending on NIHSS ≥ 6, for the comparisons of MCT, MT and SU. Chi-squared, Fisher's exact and Cochran-Mantel-Haenszel tests, as appropriated, were applied to compare ratios. For quantitative variables, the tests applied were the Student's t (two means), if a normal distribution was followed, or Wilcoxon-Mann-Whitney (two medians) alternatively. Results were assumed to be significant with a p-value < 0.05.

For multivariate analysis, we applied multiple linear regression for DT (values < 240 minutes) as outcome variable, quantile regression (Q25, Q50, Q75) for LOS, and Cox proportional-hazards model (right-censoring) along with non-parametric Kaplan-Meier estimator (log-rank test), for 1-year survival analysis. Final models were built using the stepwise method, selecting variables that had obtained differences in bivariate analysis. Estimated regression coefficients (β) were considered significant with a p-value < 0.05. Odds and hazard ratios were expressed beside 95% confidence intervals (assumed valid without value = 1). R Project for Statistical Computing (3.5.2 version) software was used for data analysis.

3. Results

We analysed 192 episodes, after removing false positives (n = 47; headache 17%,

seizures 13%, dizziness 13%, peripheral neuropathy 11%, drugs 9%, miscellanous 38%).

The cohort was categorised (Figure 1, Table 1) into TRANSFER (n = 38; 57.8% men) and NON-TRANSFER (n = 154; 51.9% women), who differed in age (67 vs. 81; $p < 0.001$), BI < 60 (2.6% vs. 18%; $p = 0.0268$), mRankin ≤ 1 (84% vs. 67%; $p = 0.0465$), Oxfordshire/Bamford LACS/PACS/POCS/TACS topographic diagnosis ratio (13/45/18/24 vs. 38/41/7/14; $p = 0.004$), AF + INR < 2 (21% vs. 13.6%; $p < 0.001$), NIHSS (6 vs. 2; $p = 0.0396$), NIHSS ≥ 6 + mRankin ≤ 1 (42% vs. 5.8%; $p = 0.0102$), alteplase thrombolysis (9 vs. 7; $p = 0.0008$), echocardiography (26% vs. 3.9%; $p = 0.0118$). Only TRANSFER, according to NIHSS ≥ 6, differed in MCT (71% vs. 29%; $p < 0.001$) and SU (80% vs. 20%; $p < 0.001$). MT was performed in 50% of TRANSFER with NIHSS ≥ 6. In evolutive analysis, there were differences in DT (146 vs. 396 min; $p < 0.001$), discharge disposition ratio after hospital admission (home 60 vs. 78, death 11 vs. 2, subacute healthcare 29 vs 20; $p = 0.01297$), LOS (6 vs. 1 days, $p < 0.001$), 30-days death in NIHSS ≥ 6 + mRankin ≤ 1 (10.5% vs. 0.6%; $p = 0.0057$), 1-year death NIHSS ≥ 6 + mRankin ≤ 1 (13.2% vs. 0.6%; $p = 0.0012$) and 1-year delta mRankin (3 vs. 1; $p = 0.0427$).

Regression models found an inverse relationship between NIHSS and DT (R^2 0.3437; $p < 0.001$), although it seems linear only when NIHSS was above 5 points (Figure 2 and Figure 3); the strongest predictor of LOS was TACS ($\beta = 3.14$ [0.03 - 8.49]; $p = 0.005$) (Table 2, Figure 4); and 1-year survival (Figure 5, Table 3) was related with TRANSFER (HR 4.68 [IC 95% 1.37 - 16.07]; $p = 0.014$), age (HR 1.1 [IC 95% 1.04 - 1.17]; $p < 0.001$), IB < 60 (HR 2.7 [IC 95% 1.02 - 7.1]; $p = 0.0447$), TACS (HR 9.82 [IC 95% 1.08 - 88.95]; $p = 0.0421$) and NIHSS ≥ 6 (HR 2.85 [IC 95% 1.05 - 7.74]; $p = 0.0401$).

In TRANSFER + NIHSS ≥ 6, MT (n = 10) was performed in 50% of cases and differences were found in MCT (71%, $p = 8E{-}5$) in addition to SU admission (80%, $p = 7.77E{-}4$).

4. Discussion

Transvictus study has allowed to describe the real-world attention of AIS/TIA patients from an unselected population, in a semi-rural community hospital.

False positives ratio was 20%, similar to other published works, although greater than in the ischemic heart disease (10% - 15%) [12]. Without a doubt, the lack of advanced neuroradiology or neurovascular specialist represents a challenge for emergency physician's clinical judgement. Although risk stratification of large vessel occlusion is possible through predictive tools that use clinical semiology, the real-world praxis of ED is characterised by overcrowding and fear to err, what could lead to not recognising false negatives and asking the expert for an assessment too soon. Perhaps internal review of the most doubtful cases and clinical simulation using standardised algorithms could improve these assumptions.

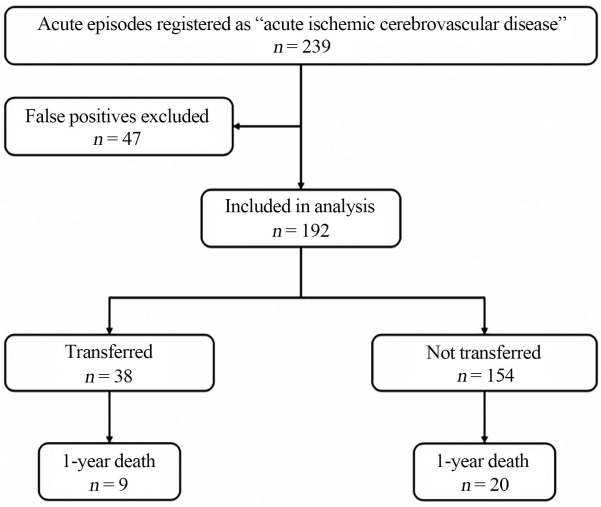

Figure 1. Flowchart of the study.

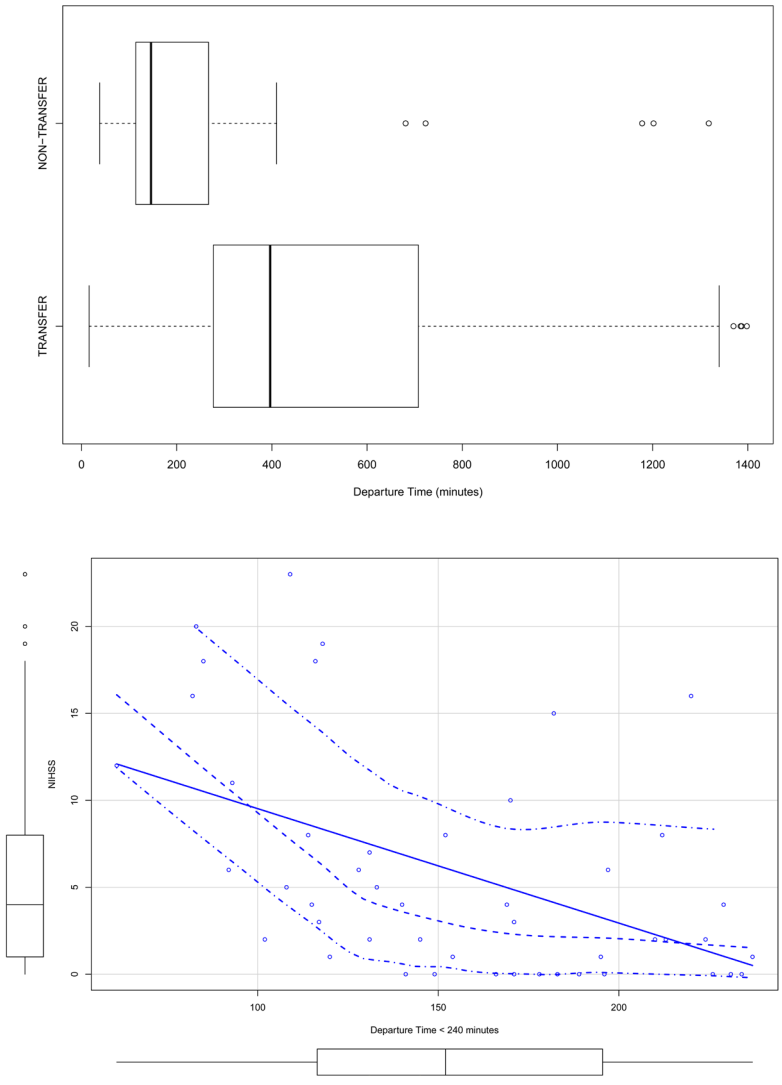

Figure 2. Analysis of Departure Time according to IFT decision and NIHSS.

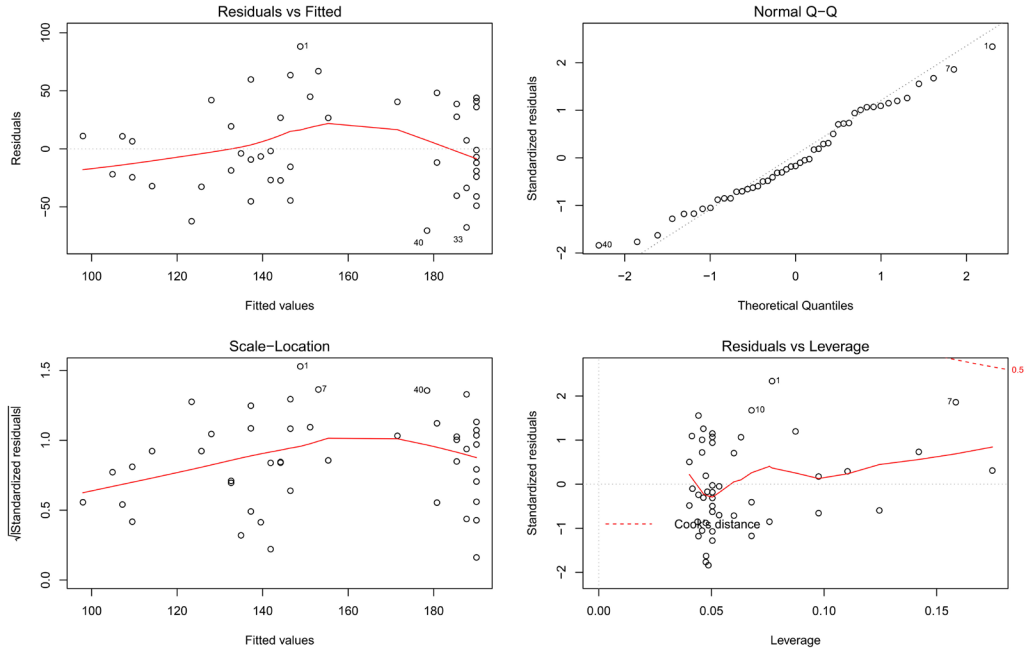

Figure 3. Simple regression for Departure Time (minutes). R^2 0.3437; p = 3.566E−05. DT = 190 − 2.3 × NIHSS − 38 × TRANSF.

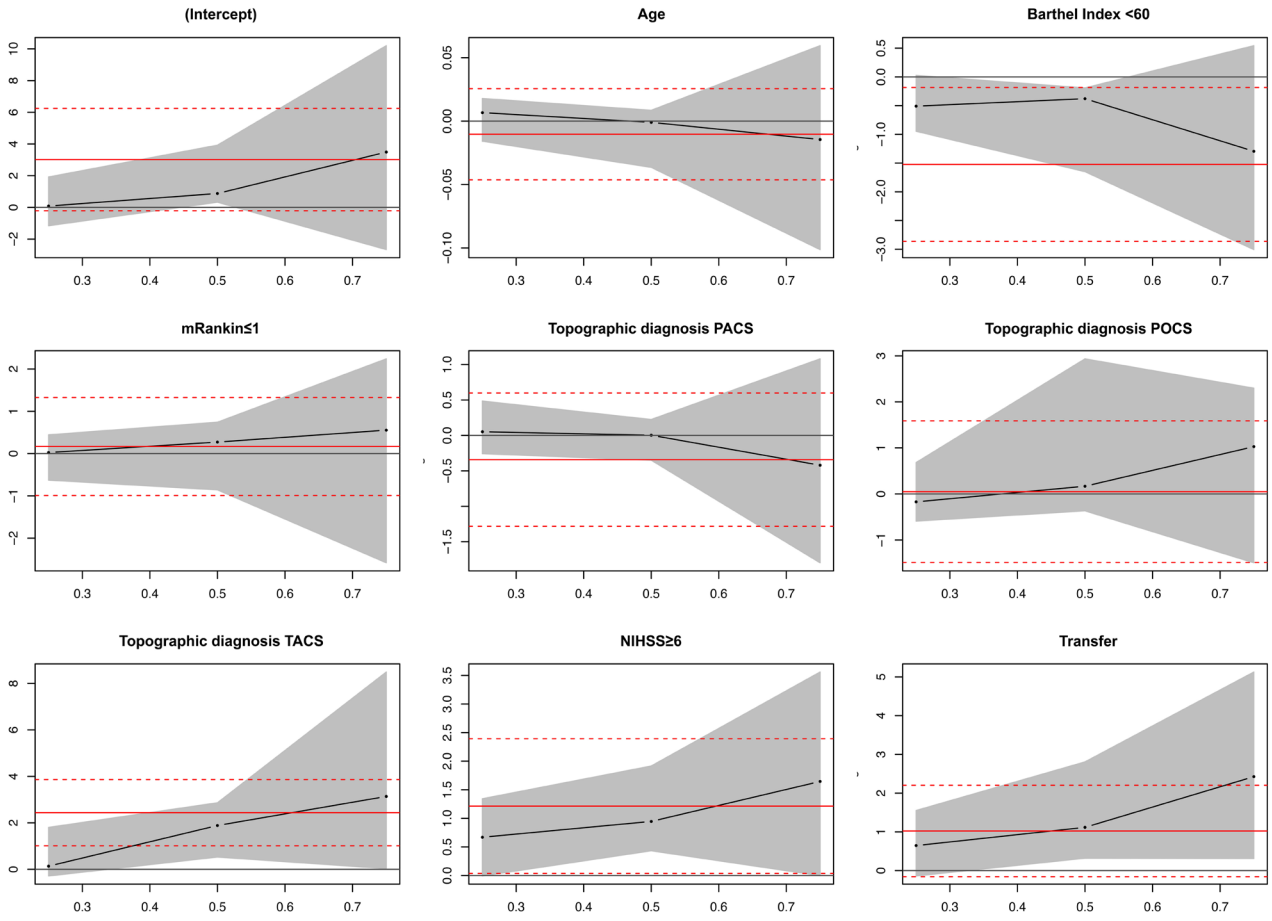

Figure 4. Plots of quantile regression for days of in-hospital stay.

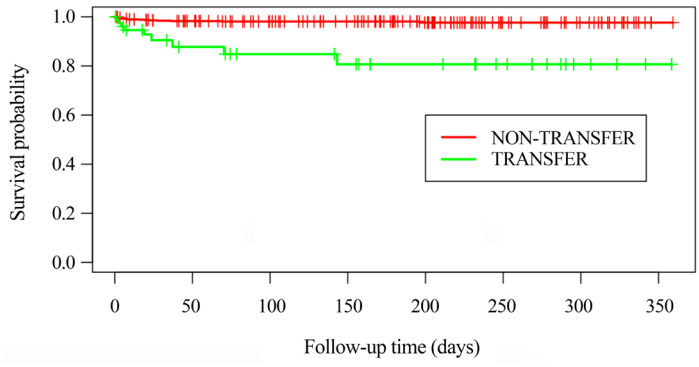

Figure 5. Kaplan-Meier survival analysis.

Table 1. Demographic and clinical characteristics of the cohort categorised according to IFT decision.

	Total (n = 192)	Transfer (n = 38)	Non-Transfer (n = 154)	p value
Demographic Data				
Age (median, IQR)	80 [66 - 86]	67 [60.5 - 80.75]	81 [68 - 87]	**0.0008**
Gender (Men/Women) %	96/96	22/16	74/80	0.3651
Functional Status and Medical History				
Barthel Index (median, IQR)	100 [78.75 - 100]	100 [96.25 - 100]	100 [66.25 - 100]	**0.0193**
Barthel Index < 60	30	1	29	**0.0268**
mRankin (median, IQR)	0 [0 - 2]	0 [0 - 1]	0 [0 - 3]	**0.0284**
mRankin ≤ 1	135	32	103	**0.0465**
Charlson Index (mean, SD)	4.45 (2.14)	3.89	4.58	0.0791
Smoke	33	9	24	0.3809
Hypertension	126	22	104	0.3526
Diabetes mellitus	47	10	37	0.9336
Dyslipidemia	74	16	58	0.7506
Cognitive impairment	40	4	36	0.1275
Atrial fibrillation	42	9	33	0.9345
Mitral valvulopathy	22	3	19	0.5764
Peripheral arteriopathy	13	0	13	0.0752
Ischemic cardiopathy	18	3	15	0.9999
acetylsalicylic acid 100 mg	53	9	44	0.6884
acetylsalicylic acid 300 mg	9	1	8	0.6911
P2Y12 inhibitors	14	1	13	0.3096
Vitamin K inhibitors	22	5	17	0.7763
Direct oral anticoagulants	7	3	4	0.1408
Angiotensin II converting enzyme inhibitors	47	6	41	0.2378
Angiotensin II receptor antagonists	19	5	14	0.5426
Lipid-lowering drugs	60	13	47	0.8070

Continued

Emergency Department Management of Stroke				
Own means, primary/prehospital/subacute healthcare %	12/43/44/1	10/29/60/0	12/47/40/1	0.1238
Topographic diagnosis (LACS, PACS, POCS, TACS, %)	33/42/9/16	13/45/18/24	38/41/7/14	**0.0041**
Atrial fibrillation	35	6	29	0.8412
International normalized ratio (median, IQR)	1.06 [1.01 - 1.14]	1.07 [1.04 - 1.18]	1.06 [1 - 1.13]	0.2262
AF + INR < 2	29	8	21	**1.205E−5**
Time of onset of symptoms (hours) (median, IQR)	2 [1 - 4.5]	2 [1 - 4.5]	2 [1 - 4.5]	0.7572
Wake-up stroke	28	8	20	0.3228
NIHSS (median, IQR)	2 [0 - 6]	6 [2 - 15]	2 [0 - 4]	**0.039**
NIHSS ≥ 6	50	20	30	**5.903E−16**
NIHSS ≥ 6 + mRankin ≤ 1	25	16	9	**0.0102**
Alteplase thrombolysis	16	9	7	**0.0008**
Supra-aortic trunks ultrasound in TIA	47	7	40	0.7279
Supra-aortic trunks ultrasound in AIS	49	14	35	0.5959
Echocardiography	16	10	6	**0.0118**
Magnetic resonance imaging	18	8	10	0.4491
Clinical Evolution Data				
Departure time from ED (minutes) (median, IQR)	345 [228 - 604]	146 [114 - 263]	396 [278 - 700]	**3.451E−5**
Disposition (home, death, subacute healthcare) %	75/4/21	60/11/29	78/2/20	**0.01297**
Emergency Department reconsultation	29	6	23	0.8628
Length of in-hospital stay (days) (median, IQR)	1.59 [0.70 - 4.92]	6.03 [3.29 - 10.55]	1.06 [0.59 - 3.22]	**3.146E−8**
30-day death	23	6	17	0.6206
30-day death (NIHSS ≥ 6 + mRankin ≤ 1)	5	4	1	**0.0057**
1-year death	29	9	20	0.2917
1-year death (NIHSS ≥ 6 + mRankin ≤ 1)	6	5	1	**0.0012**
1-year Δ Barthel Index (NIHSS ≥ 6)	10 [0 - 30]	0 [0 - 22]	22 [0 - 41]	0.2173
1-year Δ mRankin (NIHSS ≥ 6)	2 [1 - 3]	3 [1 - 5]	1 [1 - 3]	**0.0427**
Median follow-up	165.95 [50.26 - 245.87]	149.18 [26.12 - 264.52]	172.21 [56.45 - 237.80]	0.4885

Table 2. Quantile regression for days of in-hospital stay (Min. 1, Q25 0.66, Q50 1.1292, Q75 3.8106, Max. 18).

Variable		β Coefficient	95% CI		p value	Analysis of Deviance
Intercept						
	Q25	0.08617	−1.15561	1.91956	0.91635	
	Q50	0.87711	0.32970	3.92495	0.15919	
	Q75	3.49057	−2.66106	10.20243	0.16978	
Age						0.73931
	Q25	0.00669	−0.01582	0.01786	0.46417	
	Q50	−0.00095	−0.03642	0.00852	0.89063	
	Q75	−0.01451	−0.10129	0.05950	0.60737	

Continued

BI < 60					0.09845
	Q25	−0.50928	−0.94609	0.02577	0.13595
	Q50	−0.37941	−1.64902	−0.19207	0.14232
	Q75	−1.29452	−3.00532	0.54322	0.21954
mRankin ≤ 1					0.70787
	Q25	0.02500	−0.62668	0.44286	0.93238
	Q50	0.27201	−0.85739	0.74138	0.22372
	Q75	0.55417	−2.58120	2.23950	0.54295
Oxford PACS					0.57219
	Q25	0.05196	−0.25704	0.48497	0.82800
	Q50	0.00291	−0.34938	0.22445	0.98716
	Q75	−0.42039	−1.79741	1.08054	0.56960
Oxford POCS					0.61535
	Q25	−0.17254	−0.59061	0.68173	0.65933
	Q50	0.16744	−0.36747	2.93412	0.57214
	Q75	1.02749	−1.49540	2.29686	0.39595
Oxford TACS					**0.04320**
	Q25	0.13516	−0.28569	1.80260	0.70895
	Q50	1.88513	0.52886	2.86266	**<0.001**
	Q75	3.13684	0.03303	8.49063	**0.00557**
NIHSS ≥ 6					0.31600
	Q25	0.66951	−0.00717	1.34282	**0.02642**
	Q50	0.94644	0.43326	1.91522	**0.00005**
	Q75	1.64514	−0.00208	3.55895	0.07673
Transfer					0.33732
	Q25	0.64545	−0.13834	1.55109	**0.03275**
	Q50	1.11639	0.32021	2.80571	**<0.001**
	Q75	2.42533	0.31387	5.12561	**0.00966**

Table 3. Cox regression for 1-year survival after ED visit.

Variable	β Coefficient	HR	95% CI	p value
Age	0.0999	1.1	1.04 - 1.17	**0.000801**
BI < 60	0.9919	2.7	1.02 - 7.1	**0.044694**
mRankin ≤ 1	−0.9103	0.4	0.14 - 1.2	0.100278
Oxford PACS	0.9398	2.56	0.29 - 22.23	0.394218
Oxford POCS	2.008	7.45	0.63 - 88.59	0.111871
Oxford TACS	2.2846	9.82	1.08 - 88.95	**0.042150**
NIHSS ≥ 6	1.0472	2.85	1.05 - 7.74	**0.040087**
DT	−0.0008	1	0.99 - 1	0.298260

Patients with worse severity and better basal functional status were transferred, which is consistent with the recommendations of the clinical practice guidelines. However, the MCT allowed half of those transferred to be rejected for TM due to false positives, lacunar syndromes or successful reperfusion after alteplase administration. One thing that perhaps would have predicted this situation is that some of the patients with a worse initial NIHSS experienced early improvement, regardless of alteplase administration, and yet they were transferred anyway, which is also consistent with the results of other authors [13].

IFT to complement risk stratification of TIA with SAT was observed in non neglegible proportion (18%), and one of them was admitted in SU to perform carotid neurosurgery. This group of patients would probably be reduced if emergency physicians had been trained in basic neurosonology.

Severity (NIHSS) and celerity in decision making (DT) were related when adjusted according to TRANSFER (analysed DT < 4 hours). Optimisation of the functional strategy in the emergency department (early location of the patient in the examination and CT rooms, laboratory response time and periodic teleictus simulation exercises) should be an element to be considered [14]. mRankin ≤ 1 predicted worse DT, which could be explained by co-linearity with the lowest NIHSS, or TIA patients, which were observed a longer time before final disposition. LOS was shorter for non-transfer, something explainable because the goal of admission to an acute center was primarily to ensure their clinical stability, and transfer them to a subacute healthcare center in order to optimize their functional status. In contrast, transfer received many complementary examinations or invasive techniques in the acute center, which prolonged LOS.

Survival analysis showed that the prognosis of transfer was worse. This finding is very relevant for emergency medicine, as all efforts should focus on reducing the proportion of false negatives, especially of TACS, and/or higher NIHSS.

The limitations of the study are the unicentric design and the retrospective analysis, which could have caused the loss of some patients registered with an incorrect code in our computer system.

5. Conclusion

Transvictus study has allowed us to know how AIS/TIA patients are attended in the ED of a semi-rural community hospital, and the clinical process of the decision to transfer to a highly complex center. Shared decision-making with a stroke unit through telemedicine facilitated a more standardised clinical management in our non-metropolitan setting, although we identified several improvement opportunities: first, obtaining an MCT when considering an IFT, especially for the most uncertain cases; second, DT optimization of transferred patients through functional changes in ED; and thirdly, training of emergency physicians in basic neurosonology, which could improve risk stratification of TIA and therefore avoid some transfers for this reason alone.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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