**Estimating weight of acute stroke patients when dosing for thrombolysis**

Tom Barrow BSc, Muhammad S Khan MSc, Omid Halse MRCP, Paul Bentley PhD,

Pankaj Sharma MD PhD FRCP

Institute of Cardiovascular Research Royal Holloway University of London (ICR2UL) & Ashford & St Peters Hospital; and, Imperial College Cerebrovascular Research Unit (ICCRU)

**Correspondence:**

Professor Pankaj Sharma

Institute of Cardiovascular Research Royal Holloway, University of London (ICR2UL)

Royal Holloway College

Egham Hill

London TW20 0EX

Tel: +44 (0) 17 8444 3807

*No Fax number*

 pankaj.sharma@rhul.ac.uk

**Keywords:** weight, stroke, thrombolysis, prediction, dosing, rtPA

**Cover title:** Estimating thrombolysis dose by weight

**COI statement:**

The authors declare not conflict of interest.

**Author contribution**

PS devised the idea and supervised the project. TB undertook the data collection. MSK undertook the analysis. PB & OH advised and supervised on the clinical aspects. All authors contributed to the final version of the manuscript.

**Acknowledgement:**

PS is a former UK Dept of Health Senior Fellow.

**Word Count: 2156**

**Abstract**

**Background and Purpose**

Estimating patient weight forms an important part of emergency ischaemic stroke management guiding the dose of alteplase (rtPA). Weighing stroke patients can be logistically challenging and time consuming potentially delaying treatment times. We aimed to assess the reliability of approximating weight to determine rtPA dose and whether potential inaccurate dosing affected patient outcomes.

**Methods**

242 consecutive patients were studied at a large tertiary stroke centre. Estimated and actual measured weight, alteplase dose and pre and post mRS/NIHSS outcome were recorded for each patient.

**Results**

Clinicians significantly under estimated weights by 1.13kg (range -43 – +18kg, SD 7.14, p<0.05). The difference between estimated and actual weight proved to be greatest in the heaviest third of patients (-4.51kg, SD 8.35, p<0.001) resulting in 19.7% of patients receiving a deviation of at least 10% from the recommended rtPA dose. On average, the heaviest third of patients received an under-dose of 0.04mg/kg and were found to have a greater baseline NIHSS on admission (p<0.001). NIHSS improvement by day seven or upon discharge was significantly reduced in patients weighing >78kg (NIHSS score difference of 4.0 points, p<0.05) when compared to lighter individuals.

**Conclusions**

Clinicians are poor at approximating the weights of stroke patients in the acute setting, especially when patients lie at the extremes of weight. Beds capable of weighing patients should be mandated in emergency rooms for acute stroke patients.

# Introduction

Alteplase (rtPA) has a narrow therapeutic window of 4.5 hours following symptom onset with fewer symptomatic intra-cerebral haemorrhages (ICH) and reduced mortality the sooner it is administered. The recommended dose of 0.9mg/kg is limited to a maximum dose of 90mg in patients weighing ≥100kg. With necessity of time when dealing with acute stroke patients and logistics in the emergency room department clinicians commonly estimate patients' weight to determine rtPA dose.

We aimed to compare the reliability of estimating the weight of stroke patients in an acute setting with actual measured weight 24 hours later. We calculated the difference in administered rtPA dose as a consequence of the difference in estimated and actual weight. Finally, we determined if identified dosing errors caused differences in clinical outcome. This is the largest such study conducted to-date and the only study to analyse both mRS (modified Rankin Scale) and NIHSS (National Institute of Health Stroke Scale) outcome measures.

# Methods

**Data extraction**

Data from 242 stroke patients from a tertiary London stroke centre (Imperial College London, Hammersmith Hospitals, Charing Cross Hospital and St Mary’s Hospital) were analysed. Stroke specialist nurses and attending physicians estimated weight on acute presentation which determined rtPA dose. The following day, the weight of patients was formally measured using clinical ward scales and a weight estimation error calculated. Difference in alteplase dose (mg) between estimated weight and actual weight was calculated using the accepted dose of 0.9mg/kg. Outcome measures recorded were NIHSS (recorded pre-rtPA administration and 2, 24 and 72 hours and at 7 days or upon discharge) and mRS score (recorded pre-morbidly and 7 days/discharge). Improvement was calculated by subtracting scores at 7 days/discharge from admission scores.

**Statistical analyses**

Data was analysed using SPSS *v*21. A paired t-test between estimated weight and measured weight determined difference between these variables. Thereafter, univariate analysis to identify variables associated with the weight estimation error variable was undertaken. Variables found to be significant were included in a multivariable regression analysis alongside variables determined to be biologically significant (age, gender, pre-tPA NIHSS and comorbidities). The population was divided into tertiles based on measured weight and compared to one another for the weight estimation error using ANOVA.

A deviation of ±10% dose from 0.9mg/kg was used as a range for acceptable dosing of rtPA1-3 Frequencies were then obtained for patients receiving an acceptable dose of 0.81-0.99mg/kg, overdose >0.99mg or under-dose <0.81mg/kg. To investigate whether mis-dosing had an effect on functional outcome we categorised the mRS at 7 days/discharge into two separate dichotomous variables. mRS was divided into favourable outcome (0-1) and unfavourable outcome (2-6), as well as independent outcome (0-2) and dependent outcome (3-6)1-2. A binary logistic regression was then performed to ascertain any significant relationship between dosing and outcome. Dose of alteplase (mg) was calculated for both estimated weight and measured weight for each tertile group and compared with a paired t-test. Tertiles of measured weight were compared against one another for NIHSS improvement to determine any change in the magnitude of recovery between groups. Dose deviation from the optimum dose was calculated.

**Results**

Demographic details of the study population are presented in Table 1.

Clinicians underestimated mean difference weight by 1.13kg (p<0.05) between estimated (71.41 SD 14.20) and actual measured weight (72.54 SD 16.17). Results were not altered following adjustment for covariables of age, gender, pre-rtPA NIHSS, oral anticoagulants and co-morbidities using univariate and multivariate analysis.

To determine whether extremes of weight affected weight estimation, measured weight was divided into tertiles. Tertile 1 represents the lightest 81 patients weighing between 37-64.5kg, tertile 2, 80 patients weighing 64.6-77.8kg, and tertile 3, 81 patients weighing from 77.9-120kg. Table 2 illustrates that the estimated weight error for individuals in the 3rd (heaviest) tertile was significantly different from the lower tertiles (p<0.001). This association remained significant after removing patients with estimated weights greater than 100kg and following adjustment for covariables. The difference in mean weight estimation error between tertile 1 and 2 was 2.4kg (p=0.026). Similarly the difference in mean weight estimation error between tertile 1 and 3 was 7.3kg (p<0.001). To show that the margin of weight estimation error was greater at the extremes of weight, percentage error was calculated for each tertile and plotted (Supplemental Figure 1).

**Effect of estimation error on dose**

Using the range 0.81-0.99mg/kg as an acceptable dose, patients were divided into three groups: under-dose, acceptable dose and overdose. The majority of patients (80.3%) received a dose within the acceptable range. Consistent with underestimation of weight, more patients were in the under-dosed category than the overdosed category, 11.5% and 8.1% respectively.

A paired t-test was performed for each tertile of measured weight, comparing the estimated weight-based dose and the measured weight-based dose (Table 3). In the lowest and highest tertiles this difference proved to be significant (p<0.05). Patients in tertile 3 received an average dose of 77.6mg where they should have received 80.0mg, a deficit of 3.0%. By contrast, tertile 1 received 51.54mg where they should have received 50.33mg, resulting in an overdose of 2.42%. Using a dose error margin of ±10%, 7.1% of patients received an inaccurate dose (p=0.01).

**Effect of estimation error on clinical outcome**

We divided mRS at 7 days/discharge into favourable/unfavourable outcome and independent/dependent outcome. 58.1% of patients achieved a favourable outcome defined as mRS between 0-1. With an independent outcome, mRS between 0-2, this value increases to 70.0%.

Dosing groups defined as under-dosed, acceptable dose and overdosed were then analysed to determine their effect on the mRS outcomes; favourable/unfavourable and independent/dependent. Dosing errors proved to have no effect on mRS measured outcome. Dosing groups were also compared to intracerebral haemorrhage rates (ICH) but also had no effect (p=0.66)

The NIHSS score improved from 9.9 to 4.4 between admission and 7 days/discharge on average (Table 1). Improvement in NIHSS was calculated to analyse the magnitude of recovery seen in different patient groups. Dose deviation from the optimum dose of 0.9mg/kg was also calculated. A correlation was observed between measured weight and pre-tPA adjusted NIHSS score, implying that heavier patients have more severe strokes (p<0.001). Tertile 3 (heaviest) group had the largest mean deviation in dose of -0.04mg/kg and the smallest improvement in NIHSS of 4.00. Patients in tertile 2 (average) were accurately dosed with a mean deviation of -0.02mg/kg. This group saw the greatest improvement in NIHSS with 5.30 points on average. Finally, tertile 1 (lightest) patients who received an overdose of 0.03mg/kg had an improvement of 4.51. Following adjustment for age and comorbidities using multiple linear regression, patients from tertile 1 had a greater improvement in NIHSS score of 1.8 when compared to tertile 3 (p=0.048).

**Discussion**

Our analysis suggests that clinicians tend to significantly underestimate a patients' weight and this is largely accounted for by the underestimation of patients in the heaviest tertile weighing between 77.9 and 120kg, although clinicians also tended to overestimate individuals who are in the lightest tertile.

As a consequence of estimation errors, incorrect dosing could negatively impact on patient outcome (increased ICH or ineffective thrombolysis). The majority of those in our study receiving an inaccurate dose were under-dosed.

Those in tertile 2 were most appropriately dosed and saw the greatest improvement in NIHSS score. Conversely, those receiving the largest deviation in dose had a comparatively reduced improvement in NIHSS score by day 7/discharge. Heavier patients were also noted to have more severe baseline NIHSS scores, and therefore have a greater potential benefit from appropriate thrombolysis, although may derive less benefit from rtPA4 but this does not explain the reduced improvement in NIHSS score for tertile 3, which represents one-third of our population.

Other investigators have also demonstrated a large variation in the accuracy of weight estimations with clinicians possibly better at estimating weights closer to their own5. The error rate for our study population was 19.7%, which falls between two previous studies of 38.2%1 and 14.9%2. Estimating weight to determine rtPA dose is certainly more widely practiced compared to anthropometric measurements1 which can take as long as formally weighing patients.

While our study is one of the largest conducted on weight estimation in the acute stroke setting to-date and the only study to include NIHSS outcomes in addition to mRS1-3, a number of limitations need to be considered. This was a retrospective study and subject to that bias. However, the data analysed was from an extensive database of all consecutive acute stroke patients admitted no matter what time of day. We therefore believe that all patients have been captured. While weight was measured within 24 hours it may differ slightly from admission weight due to the effects of dehydration. Although weight estimation is necessary to determine tPA dose for the majority of patients, individuals weighing over 100kg receive the maximum dose and therefore weight estimation has no bearing on these individuals (and our results were preserved when these 17 patients were excluded). The study was conducted a single city, London, UK. However, this capital city houses some of the largest acute stroke units in the country admitting nearly 2000 stroke patients per year. Thus, we believe our data and results are likely to be representative of most stroke units. Finally, we would argue that those with the heaviest weight have the worst outcomes because of dosing errors, but it is possible that their outcomes were worse because of associated co-morbidity, although this was not the case in another large study addressing this issue6. Notwithstanding this evidence, being overweight could be associated with bad outcome and under-dosing may be a contributing factor to that outcome.

We conclude clinicians are poor at approximating the weights of stroke patients in the acute setting, especially at the extremes of weight. These heaviest patients, around 1 in 3 of all thrombolysed patients, tend to be under-dosed which may lead to poorer outcomes. Our results argue in favour of beds capable of weighing patients in emergency rooms for acute stroke patients who are unable to report their own weight.

**Disclosures**

None

**References**

1. Breuer L, Nowe T, Huttner HB, Blinzler C, Kollmar R, Schellinger PD, et al. Weight approximation in stroke before thrombolysis: the WAIST-Study: a prospective observational "dose-finding" study. Stroke. 2010;41(12):2867-71.

2. Messé SR, Kasner SE, Cucchiara BL, Demchuk A, Tanne D, Ouyang B, et al. Dosing errors did not have a major impact on outcome in the NINDS t-PA stroke study. J Stroke Cerebrovasc Dis. 2011;20(3):236-40.

3. Sahlas DJ, Gould L, Swartz RH, Mohammed N, McNicoll-Whiteman R, Naufal F, et al. Tissue plasminogen activator overdose in acute ischemic stroke patients linked to poorer functional outcomes. J Stroke Cerebrovasc Dis. 2014;23(1):155-9.

4. Lou M, Selim M. Does body weight influence the response to intravenous tissue plasminogen activator in stroke patients? Cerebrovasc Dis. 2009;27(1):84-90.

5. Coe TR, Halkes M, Houghton K, Jefferson D. The accuracy of visual estimation of weight and height in pre-operative supine patients. Anaesthesia. 1999;54(6):582-6.

6. Doehner W, Schenkel J, Anker SD, Springer J, Audebert HJ. Overweight and obesity are associated with improved survival, functional outcome, and stroke recurrence after acute stroke or transient ischaemic attack: observations from the TEMPiS trial. European heart journal. 2013;34(4):268-77.

|  |
| --- |
| **Table 1: Descriptive statistics for stroke patients (n=242)** |
|  |  |
| **Variables** | n(%) |
| Age, mean (SD) | 71.2 (16.3) |
| Gender, male (%) | 123 (50.8) |
| Thrombectomy (%) | 7 (2.9) |
| **Risk Factors, yes (%)** |  |
| Hypertension | 143 (59.1) |
| Diabetes | 46 (19) |
| Hyperlipidaema | 70 (28.9) |
| Current smoker | 29 (12) |
| Previous smoker | 43 (17.8) |
| Previous ischaemic stroke | 54 (22.3) |
| Atrial fibrillation | 35 (14.5) |
| Congestive cardiac failure | 13 (5.4) |
| **Medications, yes (%)** |  |
| Aspirin/dipyridamol | 58 (24) |
| Clopidogrel/other antiplatelet | 28 (11.6) |
| Anticoagulants | 10 (4.1) |
| Antihypertensive | 48 (19.8) |
| **Observations on admission, mean (SD)** |  |
| Systolic Blood pressureΒ | 153.1 (27.5) |
| Diastolic Blood pressureΒ | 80.9 (16.9) |
| GlucoseΓ  | 7.4 (2.8) |
| **NIHSS score, mean (SD)** |  |
| pre-tPAΔ | 9.9 (6.8) |
| After 2 hoursΕ | 7.4 (6.9) |
| At 24 hoursΖ | 6.2 (6.6) |
| At 72 hoursΗ | 5.4 (6.5) |
| At 7 days/dischargeΘ | 4.4 (6) |
| **mRS score, frequency** |  |
| **Pre-morbidΙ** |  |
| 0 | 192 |
| 1 | 17 |
| 2 | 11 |
| 3 | 14 |
| 4 | 6 |
| **7 day/dischargeΚ** |  |
| 0 | 66 |
| 1 | 60 |
| 2 | 26 |
| 3 | 20 |
| 4 | 34 |
| 5 | 9 |
| 6Intracerebral Haemorrhage (ICH)L | 117 (0.07) |
| B n=241, Γ n=236, Δ n=238, Ε n=235, Ζ n=234, Η n=197, Θ n=204, Ι n=240, Κ n=216 L n=234 |

**Table 2: Comparison of weight estimation error for tertiles of measured weight using ANOVA (n=242)**

|  |
| --- |
| Tukey's Honest Significant Difference & Lowest Significant Difference analysis |
| **Measured Weight (kg)** | Tertile 1mean diff (p value) | Tertile 2mean diff (p value) | Tertile 3mean diff (p value) |
| **Tertile 1 (37-64.5)** |  | 1.56 (0.307) | 5.86 (<0.001) |
| **Tertile 2 (64.6-77.8)** | -1.56 (0.307) |  | 4.30 (<0.001) |
| **Tertile 3 (77.9-120)** | -5.86 (<0.001) | -4.30 (<0.001) |  |
| Least Significant Difference |
| **Measured Weight (kg)** | Tertile 1mean diff (p value) | Tertile 2mean diff (p value) | Tertile 3mean diff (p value) |
| **Tertile 1 (37-64.5)** |  | 1.56 (0.143) | 5.86 (<0.001) |
| **Tertile 2 (64.6-77.8)** | -1.56 (0.143) |  | 4.30 (<0.001) |
| **Tertile 3 (77.9-120)** | -5.86 (<0.001) | -4.30 (<0.001) |  |

**Table 3: Paired t-test between theoretical dose based on measured weight compared to dose based on estimated weight for tertiles of measured weight (n=242)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Measured weight (kg)** | **Dose based on estimate (mg)** | **Dose based on measured (mg)** | **P value** |
| **Tertile 1 (37-64.5)** | 51.54 | 50.33 | 0.041 |
| **Tertile 2 (64.6-77.8)** | 63.64 | 63.83 | 0.745 |
| **Tertile 3 (77.9-120)** | 77.62 | 80.03 | 0.001 |