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Assessment of Long Term Outcomes for the STRokE DOC Telemedicine Trial (STRokE DOC-LTO)

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Abstract

Goal—Telemedicine can provide stroke evaluations to areas with limited available expertise. Telestroke reliability has been established. Decision-making efficacy has been shown in the STRokE DOC trial. No prospective trial has assessed long term telestroke outcomes.

Materials and Methods—In an IRB approved trial (NCT00936455), we contacted patients originally enrolled in the NIH STRokE DOC trial. A telephone script was used to verify consent. Patients were asked standardized questions of disposition, mRS, mortality and recurrent stroke for 2 retrospective time points (6 & 12 months after event) and 1 current time point. Blind was maintained. Primary outcome measures of mortality and %mRS(0-1) at 6 months are reported. The Wilcoxon Rank-Sum was used for continuous variables and Fisher's Exact was used for categorical variables.

Findings—Of the original 222 participants, 75 patients or surrogates were able to be contacted. Time from enrollment was 3.96 ±1.0 years (Min 2.33,Max 5.45). Mean NIHSS score was 8±7 (5±8 telephone, 12±8 telemedicine; p=0.002). IV rt-PA rate was 31%. Six month mRS(0-1) outcomes were not different at 42%. Mortality after imputing to entire study sample was not different at 18%. There was no difference in recurrent stroke (p=0.61). Eighty-six percent reported being home at 6 months.

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Conclusions—This study reports a good 6 month outcome for stroke patients evaluated by telemedicine or telephone. This design is limited by time since original enrollment and resultant inability to contact participants. Though this study can add to the limited data on telemedicine outcomes, a prospective trial is needed.

Keywords

Stroke; Telemedicine; Telestroke; Outcome; Assessment

Introduction

The problem of emergency access to acute healthcare is significant for disorders such as myocardial infarction, sepsis, trauma, and stroke.1 In a condition such as stroke, where minutes matter and delay results in poorer outcomes and tissue loss, optimizing access to care can not be overemphasized.2,3 rt-PA rates continue to be low.4–6 With system level improvements, rt-PA rates increased from 14% to 37.5% in larger academic hospitals.7 This benefit may not be seen in all geographic locations or facility types. Sixty-four percent of hospitals assessed reported no stroke rt-PA treatments over 2 years, with these hospitals tending to be smaller and in less densely populated areas.8

Telemedicine is one potential solution to the problem of limited expertise availability. Telemedicine could facilitate remote consults, shorten hospital stays, avoid unnecessary transfers, enhance education, and improve research trial enrollments.9,10 Telestroke's reliability has been reported11–15 leading to the Class I, Level A recommendations regarding reliability.16 Feasibility has been extended to usability with the development of newer web-based designs, site independent assessments, and mobile robotic units.17–20 Telemedicine rt-PA rates have increased by 10 fold with some centers reporting rates of up to 30%.19,21–25

Efficacy for decision-making has been shown in the STRokE DOC telemedicine vs. telephone trial. Some data is now available showing good 6 month outcomes.21 To date, no large scale, prospective, randomized trial has assessed the long term outcomes of stroke patients evaluated via telemedicine. The STRokE DOC-LTO trial follows patients evaluated in the original trial, and is one means to further assess outcomes while awaiting a prospective long term outcomes study.

Materials & Methods

The original STRokE DOC trial design has been published.18 STRokE DOC was an NIH funded, prospective, multi-site, randomized trial comparing the decision-making efficacy of two consultation techniques. Patient underwent either a telemedicine or telephone-only consultation, with cases reviewed at 3 levels of data availability. Primary outcomes showed correct 98% decision-making efficacy for telemedicine and 82% for telephone. Mortality at 90 days was not different between groups but was not a primary outcome. The original trial did not include 6 or 12 month assessments.19

In this retrospective, IRB approved STRokE DOC-LTO trial (NCT00936455), we contacted patients originally enrolled in that STRokE DOC trial. One of 5 UC San Diego Stroke Specialists attempted telephone contact to these patients. A telephone script, approved by the Human Research Protections Program, was used to verify consent, ensure standardization of questions, and maintain original blind. Upon patient or surrogate contact and approval, participants were asked a series of standardized questions related to disposition, modified Rankin Scale Score (mRS), mortality and whether or not the patient

had suffered a recurrent stroke for 2 retrospective time points (6 & 12 months after event) and 1 current time point. Given the time since event, the mRS was simplified to assess only the extremes of function. Patients without any signs or symptoms were “asymptomatic” (0 on mRS). Patients reporting mild symptoms only were “mild” (1 on mRS). Any more significant deficits affecting function, in alive patients, would be “more severe” (2-5 on mRS). If informed of death, date of death was ascertained and patient was recorded as a “death” (6 on mRS). Investigators were not given information regarding the patient’s original randomization allocation. During telephone contact, investigators were precluded from asking any questions in an attempt to determine original randomization.

Primary outcome measures were mortality and percentage of patients with mRS(0-1) at 6 months. Information regarding mortality and mRS at 12 months after initial event was also recorded. Finally, since the telephone contact was done at 1 specific time point (variable length of time for each patient from trial enrollment), a combined “current time” assessment of mortality and mRS was obtained. The Wilcoxon Rank-Sum was used for continuous variables and the Fisher’s Exact was used for categorical variables. Since this is an exploratory analysis, no adjustments were made for multiple comparisons and a p-value < 0.05 was considered significant. Statistical analysis was done using the statistical software R (version 2.9.0).

Given the significant length of time since original enrollment in the STRokE DOC trial, not all patients could be contacted. An imputation strategy was used to assess mortality given limited contact ability. Of the original 222 patients, 35 had known death within 90 days. Out of the remaining 187 patients, 75 were contacted successfully. To estimate the overall mortality in the original population we assumed that the contacted patients would be representative of the whole population. The mortality rate found in the contacted patients was thus used for imputation.

Results

Table 1 notes patient baseline characteristics. Of the original 222 participants, 35 had a death within the specified trial period. Of the resulting 187, 75 patients or surrogates were able to be contacted (38 telephone, 37 telemedicine). The mean time from original enrollment to contact for STRokE DOC-LTO was 3.96 years (Min 2.33,Max 5.45). Mean age was 67±13 years. Fifty-five percent were male (p=0.65). Ninety- three percent were white (p=0.49). Thirty-nine percent were Hispanic (p=0.82). Risk factors analysis showed no differences for coronary artery disease (p=0.49), myocardial infarction (p>0.99), family history of TIA or stroke (p=0.11), history of atrial fibrillation (p=0.12), history of diabetes (p>0.99), or prior history of cerebrovascular disease (p=0.06). For alcohol use, there were more telephone patients having reported use (16% overall, 24% telephone, 8% telemedicine; p=0.003) while for tobacco use there were more telemedicine patients having reported use at time of index event (11% overall, 5% telephone, 16% telemedicine; p=0.02). Both risk factors had a high percentage of data collection “unknowns” (23% for alcohol use and 24% for tobacco use) which may have driven the statistical significance. Baseline NIHSS score was 8±7 with increased severity in telemedicine (5±8 telephone, 12±8 telemedicine; p=0.002) consistent with the original trial. Baseline mNIHSS was 6±6 (4±7 telephone, 9±7 telemedicine; p=0.004). Pre-stroke dichotomized mRS (0-1) was not different (p=0.56), nor was baseline dichotomized mRS (0-1) (p=0.27). Overall IV rt-PA rate was 31% (p>0.99).

As noted in Table2, the primary outcome measures of 6 month mRS and mortality did not show differences between groups. Six month mRS(0-1) outcome was 42% (50% telephone, 34% telemedicine; p=0.23). Six month mortality after imputing to the entire study sample (n=222) was 18% (15% telephone, 21% telemedicine; p=0.38).

Secondary outcomes were also reported. There was no difference in reported 6 month recurrent stroke at 4% (p=0.61). Eighty-six percent reported being home at 6 months (p=0.31). Dichotomized 12 month mRS and 12 month mortality did not show differences between groups. Twelve month mRS(0-1) outcome was 44% overall (53% telephone, 36% telemedicine; p=0.23). Imputed 12 month mortality was 21% (17% telephone, 25% telemedicine; p=0.19). There was no difference in reported recurrent stroke at 6-12 months at 1% (p=0.49). Ninety-One percent reported being home at 12 months (p>0.99).

There were 23 patients in the rt-PA subset (12 telephone, 11 telemedicine). There were no differences in gender, race, ethnicity, CAD, MI, family history, atrial fibrillation, alcohol, tobacco, pre-stroke mRS or baseline mRS. There were more diabetics (33% telephone, 73% telemedicine; p=0.04) and more prior strokes (33% telephone, 73% telemedicine; p=0.04) in telemedicine. Baseline NIHSS score was 12±7 (9±7 telephone, 15±7 telemedicine; p=0.06). Six month mRS(0-1) outcome was 35% (44% telephone, 27% telemedicine; p=0.64). There were no new deaths reported in this rt-PA subset between 90 days and 6 months in either group.

Discussion

Recent database information supports the safety and feasibility of “drip and ship” rt-PA models by showing similar discharge status whether treated at the outside spoke hospitals and then transferred, or treated at the hub centers directly.26 Other investigators have shown good outcomes of patients when combining stroke wards, education initiatives, and telemedicine.27 Data also shows good long term outcomes at 6 months. 21 Those non-randomized reports are integral to the understanding of telemedicine’s use in a systems of care model.16,28

The STRokE DOC trial showed telemedicine efficacy for medical decision-making.19 That trial was not powered to assess 90 day functional outcomes or mortality. This STRokE DOC-LTO study adds more data for our understanding of long- term patient outcomes. Our 6 month assessments show an overall mortality of 18% (15% vs. 21%) and mRS(0-1) of 42% (50% vs. 34%). Our report that there was no statistical difference between telemedicine and telephone for mortality or functional outcomes may add credibility to using either telephone or telemedicine modality to safely assess stroke patients. This will need to be verified in a prospective comparison.

The mortality (21%) and mRS (34%) data for telemedicine, are in line with other telemedicine assessments showing 6 month telemedicine rt-PA mortality of 14% and mRS(0-1) of 40%, though there were too few rt-PA patients contacted in our sample to make a significant comparison of only the rt-PA subset (as only 9 patients in the sample had 6 month outcomes).21 Further evidence that telemedicine results in good long term outcomes is shown by 86% (91% telephone, 80% telemedicine) of participants being “home” at 6 months after the stroke.

This trial is limited by the retrospective design, small number of patients contacted, significant time since original enrollment, recall bias, and imputation choice to estimate mortality in entire population based on assumption that contacted patients were representative of the whole.

Only 40% of the original cohort’s patients were able to be contacted. Though this is less than the contact rate for other trials, our assessment was done many years after initial enrollment making a lower contact rate more likely. 21,29 There were approximately equal numbers in each trial arm, and both demographic and risk factor data were consistent with the original STRokE DOC trial, helping assure that a representative sample of the overall

trial was assessed.19 There was a significant time from initial enrollment which most likely would have influenced self reporting of abilities at specific time points, with resultant recall bias. It is unlikely that this delay or patient recall bias affected the binary choice of alive or dead making these values reliable. Owing to the clinical trial design choice to simplify functional outcome questioning, such as grouping most deficits of mRS 2-5 into a single category of “more severe” and choosing to report only the dichotomized mRS category of (0-1), limits much of the effect of patient recall bias. Reporting, in essence, was limited to knowing whether the patient was alive or dead, or asymtopmatic/ mild symptoms or “more severe”. Although we have chosen to also report out the “current” mortality and functional outcome measures, the variable time from enrollment of 3.96 years (Min 2.33, Max 5.45) makes interpreting this information somewhat more complex.

There is likely a recall bias for whether patients had a recurrent stroke. Chart review was beyond to scope of this assessment, and would not have captured data from other hospitals. Our study also does not account for small strokes that the patient may have forgotten about, or never even knew about, based on imaging that may have been done. Although likely underreported, this bias is equally applied to both of the randomization groups.

Our choice to use one of many possible imputation strategies to account for the limited contact is one of our stated limitations. Although other imputation strategies can be assessed, the authors feel that given the limitations of the data, the best action would be to pursue a prospective assessment in a randomized trial.

Overall, the data presented in this STRokE DOC-LTO trial is comparable to other reports showing favorable 6 month telemedicine functional outcomes and mortality. Though this study can add to the data on telemedicine outcomes, limitations should be addressed with a prospective trial assessing long term patient outcomes.

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Table 1

Baseline Patient Characteristics

Baseline patient characteristics presenting demographics, co-morbid conditions, risk factors, degree of deficit, treatments and time from initial trial enrollment.

Criteria	Overall (N)	Telephone (N)	Telemedicine (N)	*P* Value
Age (in years)				
Mean ± SD	67±13 (75)	67±13 (38)	68±13 (37)	0.61
Weight (in kg)				
Mean ± SD	83±16 (58)	82±18 (26)	83±18 (32)	0.39
Sex				
Male %	55 (41)	58 (22)	51 (19)	0.65
Female %	45 (34)	42 (16)	49 (18)	
Race				
Asian %	1 (1)	3 (1)	0 (1)	0.49
Black %	5 (4)	3 (1)	8 (4)	
White %	93 (70)	95 (36)	92 (70)	
Ethnicity				
Hispanic %	39 (29)	37 (14)	41 (15)	0.82
Not Hispanic %	61 (46)	63 (24)	59 (22)	
Risk Factors				
Coronary Artery Disease %	21 (16)	18 (7)	24 (9)	0.49
Myocardial Infarction %	7 (5)	8 (3)	5 (2)	>0.99
Family Hx of TIA/Stroke %	15 (11)	8 (3)	22 (8)	0.11
Atrial Fibrillation %	12 (9)	5 (2)	19 (7)	0.12
Diabetes Mellitus %	36 (27)	37 (14)	35 (13)	>0.99
Cerebrovascular Disease %	41 (31)	53 (20)	30 (11)	0.06
Current Alcohol Use %	16 (12)	24 (9)	8 (3)	0.003†‡
Current Tobacco Use %	11 (8)	5 (2)	16 (6)	0.02†‡
Clinical Features				
Baseline NIHSS ± St.Dev	8±7 (75)	5±8 (38)	12±8 (37)	0.002†
Baseline mNIHSS ± St.Dev	6±6 (75)	4±7 (38)	9±7 (37)	0.004†
Prestroke mRS (0-1) %	81 (60)	84 (32)	78 (28)	0.56
Baseline mRS (0-1) %	23 (17)	29 (11)	16 (6)	0.27
Treatment with rt-PA				
No %	69 (52)	68 (26)	70 (26)	>0.99
Yes %	31 (23)	32 (12)	30 (11)	
Time from Enrollment to Contact (in years)				
Mean ± SD	4±1 (74)	4±1 (37)	4±1 (37)	0.69

† Denotes statistical significance with P < 0.05

††Denotes a high percentage of “unknowns” which may have driven the statistical significance.

Table 2

Patient Outcomes

Patient Outcomes table showing co- primary outcome measures of 6 month functional outcome (dichotomized mRS(0-1)) and 6 month mortality rates. Also included are secondary measures for 6 month self report of recurrent stroke and patient disposition. Similar reports for 12 months and "current" time of contact are also shown. Baseline NIHSS and 6 month mortality also noted for rt-PA subset.

Outcome	Overall (N)	Telephone (N)	Telemedicine (N)	*P* Value
Primary Outcomes				
6 month mRS (0-1) %	42(29)	50(17)	34(12)	0.23
6 month mortality % [non-imputed]	3(2)	3(1)	3(0)	>1.99
6 month mortality % [imputed]	18(40)	15(17)	21(23)	0.38
Secondary Assessments				
6 month recurrent stroke %	4(3)	6(2)	3(1)	0.61
6 month disposition "Home" %	86(59)	91(31)	80(28)	0.31
6 month disposition "Other" %	14(10)	9(3)	20(7)	0.31
12 month mRS (0-1) %	44(31)	53(18)	36(13)	0.23
12 month mortality % [non-imputed]	7(5)	5(2)	8(3)	0.67
12 month mortality % [imputed]	21(47)	17(19)	25(28)	0.19
6-12 month recurrent stroke %	1(1)	3(1)	0(0)	0.49
12 month disposition "Home" %	91(64)	91(31)	92(33)	>0.99
12 month disposition "Other" %	9(6)	9(3)	8(3)	
"Current" mRS (0-1) %	36(27)	38(14)	35(13)	>0.99
"Current" mortality % [non-imputed]	22(16)	27(10)	16(6)	0.40
"Current" mortality % [imputed]	34(76)	36(40)	32(36)	0.67
12 month- "Current" recurrent stroke %	11(8)	17(6)	6(2)	0.15
"Current" disposition "Home" %	76(56)	68(25)	84(31)	0.18
"Current" disposition "Other" %	24(18)	32(12)	16(6)	
rt-PA Subset Analysis				
Baseline NIHSS ± St.Dev	12±7 (23)	9±7 (12)	15±7 (11)	0.06
6 month mRS (0-1) %	35(7)	44(4)	27(3)	0.64
6 month mortality % [imputed]	*Unable to Impute*	*Unable to Impute*	*Unable to Impute*	*Unable to Impute* †

† Unable to Impute due to no patients having reported death between end of study (90 days) and 6 month followup.