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Telestroke, teleoncology and telenephrology: a systematic review to analyse the outcomes of active therapies delivered with telemedicine support to manage strokes, cancer and chronic kidney disease.

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Summary:

Mortality and morbidity is significantly higher in rural and regional areas due to various factors including a deficiency in the availability of specialist care leading to later diagnosis and delays in treatment. Telemedicine attempts to address some of these issues. The main fields that deliver medical therapies through real time videoconference (VC) are oncology for chemotherapy, neurology for stroke thrombolysis and nephrology in supervising haemodialysis (HD). This review studies the effectiveness of these telemedicine models in terms of patient outcomes and satisfaction. This systematic review involved a search of MEDLINE, CINAHL and INFORMIT databases using key terms. 563 articles on telemedicine were found; from these 67 full texts were perused yielding 8 articles for telestroke, 3 for telenephrology and 2 for teleoncology. Observational studies conducted in the field of telestroke have shown favourable outcomes when comparing face to face and VC aided thrombolysis with no significant disparity between survival and intra-cerebral bleeds between the two cohorts. HD supervised through VC also showed no change in patient outcomes when compared to HD at dialysis centers. Evidence regarding the efficacy of using real time VC for infusion delivery is however limited. Administering active therapeutic interventions seems feasible given the presence of certain factors at the rural sites such as CT scanning facilities for stroke management, chemo-competent nurses to deliver chemotherapy and dialysis nurses.

Keywords: telemedicine, videoconference, stroke, thrombolysis, chemotherapy, oncology, renal, dialysis.

Introduction

Cancer is responsible for about 29% of all deaths in Australia and up to 25% of excess deaths in regional areas. In regional areas death rates are 10% higher for males and about 5% higher for females than in major cities.(1) Such disparity in health outcomes for cancer between urban and regional populations can be attributed to later date of diagnosis, poorer access to health care, different health seeking behaviour, health workforce shortages in regional areas (especially amongst specialists) and higher Indigenous population.(1) Cancer risk factors such as smoking, obesity and alcohol consumption are also higher in rural and regional populations.(2)

To overcome barriers and improve access to oncology treatments various models have been instigated in regional and rural areas, such as face to face outreach clinics or more recently telehealth models.(3) One of the longest running teleoncology services, first established in 1995, is in Kansas. This has demonstrated success by incorporating more rural sites under its service and also reducing the cost of delivery.(4) Teleoncology has also secured its roots in nations such as Canada, UK and Scotland where health resources are concentrated in major cities but the population is dispersed over a large area.(5, 6) Many existing telehealth models across Australia and other developed nations have focused on providing consultations and follow up for their regional and rural patients, where most patients continue to travel to larger centers for treatment. Few medical specialties have embarked on remotely supervising active medical therapies via Real Time (RT) videoconference (VC) to provide a more comprehensive service closer to home. Stroke, cancer and kidney disease management are areas where telemedicine has progressed to supervising active treatment through providing thrombolysis, chemotherapy and dialysis via VC. Thus, this review will aim to explore the outcomes of using telemedicine supervision to deliver active therapeutic treatment to rural patients in the fields of stroke, medical oncology and nephrology (widely known as telestroke, teleoncology and telenephrology respectively).

Methods

A systematic review was conducted applying the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.(7) Computerised literature searches were performed using the terms telemedicine AND oncology, telemedicine AND "medical oncology" and telemedicine AND stroke, telemedicine AND renal or kidney/s or dialysis with language restricted to English. These searches were performed on MEDLINE, Cumulative index of nursing and allied health literature (CINAHL) and INFORMIT databases. Some articles were also identified by reviewing the bibliographies and search terms of selected articles.

Inclusion criteria were the following: articles that utilised models of telehealth to actively deliver treatment to rural, regional or remote patients as chemotherapy, thrombolytic infusions or dialysis (as these were three major areas where therapeutic interventions have begun to be administered by VC as determined by prior preliminary searching of MEDLINE and expert advice from consultants within the fields). Articles also had to assess patient outcomes and/or satisfaction from delivering therapeutic infusions via telemedicine in a scientifically valid manner. In addition studies were required to clearly explain the models used to deliver the treatment. Only observational studies and randomised controlled trials would be included in an attempt to ensure the assessment of patient outcomes was objective.

The exclusion criteria required rejection of articles that solely described the various telemedicine models, their description and details about technical feasibility. Articles that utilised telemedicine for consultations, follow-up clinics or specialist reviews and did not include providing treatment were excluded. Telemedicine for follow-up appointments after provision of thrombolysis, chemotherapy or pre/post dialysis was also excluded. Telepsychology and telerehabilitation of cancer and stroke patients were excluded. Letters, conference proceedings, editorials were also excluded.

Initial screening of articles was based on review of their titles followed by abstracts. All abstracts were read by the primary author independently, and selection of relevant articles relied on the abstracts fulfilling the inclusion criteria. Full length articles within the last 15 years were then perused to assess for eligibility according to the inclusion and exclusion criteria. Final articles were selected in accordance and after formal meeting with the supervising author and consultant. Data extraction forms and tables were developed and data was extracted and reviewed by three authors. Critical assessment of possible sources of bias and confounding in the studies was undertaken. Study results and effect sizes were also extracted and compared where possible.

Results

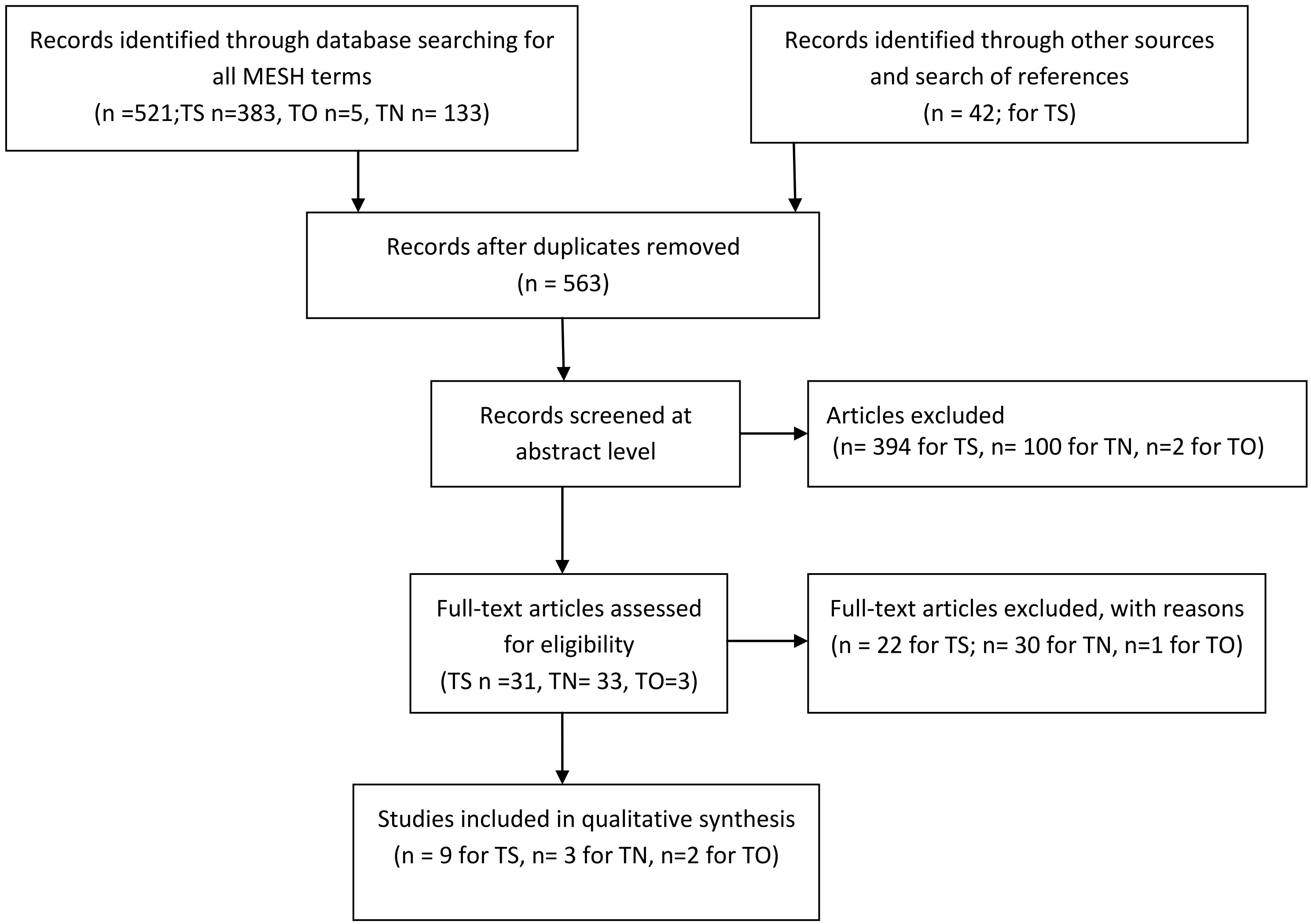
Records identified through database searching for all MESH terms
(n =521;TS n=383, TO n=5, TN n= 133)
Records identified through other sources and search of references
(n = 42; for TS)
Records after duplicates removed
(n = 563)
Records screened at abstract level
Articles excluded
(n= 394 for TS, n= 100 for TN, n=2 for TO)
Full-text articles assessed for eligibility
(TS n =31, TN= 33, TO=3)
Full-text articles excluded, with reasons
(n = 22 for TS; n= 30 for TN, n=1 for TO)
Studies included in qualitative synthesis
(n = 9 for TS, n= 3 for TN, n=2 for TO)

Figure 1: The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) flow diagram.(7) TS= telestroke, TO= teleoncology, TN= telenephrology

521 articles dealing with all forms of telemedicine were found on MEDLINE of which 394 articles included telestroke and all forms of stroke diagnosis, evaluation, investigation and management via telemedicine. 394 abstracts were reviewed from which 31 articles were chosen, those excluded either did not utilize telemedicine for direct stroke management or the study design was substandard in nature. 31 full texts were perused in detail finally yielding eight articles fit to be included in this review. The process is depicted in the flow chart above. 23 articles were excluded due to: 1) lack of administration of therapeutic thrombolytic infusion and managing stroke more passively with observation, anti-platelet therapy and other medication regimens or 2) articles that focused on stroke rehabilitation and psychosocial therapy or due to 3) limitations in study design including case studies, letters and so on.

The second search was conducted in the field of medical oncology and yielded five articles from which two were chosen and three excluded as they did not have appropriate information on patient outcomes or satisfaction rates. From the 133 articles identified in telenephrology only 3 met the inclusion criteria and were hence selected for this review.

Table 1- Quality Assessment Table-Risk of bias assessment using the Cochrane risk of bias tool (8)

Bias domains	Chowdhury 2013 (9)	Zaidi 2011 (10)	Johansson 2011 (11)	Khan 2010 (12)	Audebert 2006 (13)	Pedragosa 2009 (14)	Meyer 2008 (15)	Sairanen 2011 (16)	Schwab 2007 (17)
Study Design	Retrospective cohort study comparing FTF with telemedicine model.	Retrospective cohort comparison between spoke sites and the hub. FTF care at hub and telemedicine were provided by the same neurologist	Retrospective cohort comparison between peripheral hospitals and stroke centre	Single centre case series	Retrospective, Comparison of outcomes pre and post implementation of telestroke services	Randomised controlled study of telemedicine vs. telephone decision making and supervision of tPA	Prospective cohort study. Comparing outcomes at community hospitals with hub	Prospective cohort study. Comparing outcomes at community hospitals with hub	Prospective cohort study. Comparing outcome between regional and stroke centres
Randomisation	No	No	No	No	No	Yes	No	No	No
Allocation concealment	No	No	No	No	No	No	Yes	No	No
Blinding	No	No	No	No	No	No	No	No	No
Incomplete outcome data	No	No	No	Yes	No	No	No	No	No

Selective outcome reporting	No	No	No	Unclear	No	No	No	No	No
Other	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Risk of bias	Unclear	Unclear	Unclear	High	Low	Low	Low	High	Low

Using the Cochrane risk of bias tool, Table 1 depicts that most studies utilized did not undertake randomization, allocation concealment or selective outcome reporting making their risk of bias high or unclear. But most, except one study satisfactorily reported complete outcome from the data analyzed. From the four out of nine studies that were deemed to be at low risk of bias, one was randomised, the other had allocation concealment and all four reported complete patient outcomes. The risk of bias from others was high or unclear as they did not fulfill the major criteria. Table 2 summarises the studies selected, their study designs and outcomes reported in each study.

Table 2: Summary of articles describing the stroke management setting, study design and outcome

Reference	Country	Setting	Study design	Interventions at remote sites	Participants	Outcomes
Chowdhury 2013(9)	UK	Single stroke centre	Retrospective cohort study	Evaluation and tPA via real time VC	97 patients were thrombolysed; 46% were via telemedicine	●Intracranial bleed: FTF 7.7% vs. telemedicine 4.4% (NS), ●3 month FO: FTF 36.5% vs. telemedicine 42%(NS), ●Process times significantly shorter for face to face. E.g. admission to treatment median 33min vs. 61 min.
Zaidi 2011(10)	USA	12 spoke sites and 1 stroke hub	Retrospective cohort	Evaluation and tPA via real time VC	Number of patients: telemedicine 83, FTF 59,	●3 month FO: 42% vs. 37.5% (NS) ●No difference in ICB ●Arrival to treatment: mean 68 min vs. 90 min($p<0.01$), ●3 month mortality 30% vs. 31%.
Johannson 2011 (11)	Austria	Peripheral hospitals 20 -129 km away and stroke unit	Retrospective cohort	Evaluation and tPA via real time VC followed by transfer to stroke unit	Number of patients: Periphery 47 , stroke centre 304,	●ICB 6.4% vs. 7.6% (NS), ●3 months FO 47% vs. 43% (NS), ●3 month mortality 19% vs. 13% (NS)
Khan 2010 (12)	Canada	7 remote hospitals and 1 hub	Single centre case series	Evaluation and tPA via real time VC or telephone	At 2 years, 50 patients received telemedicine review	●At 2 years, 50 patients received telemedicine review, ●tPA within 3 hours 73%, ●ICB 11.4%, ●3 month mortality 22.5%, ●3 month FO 40%, ●92.5% decline in transfer rate.
Audebert 2006 (13)	Germany	12 regional clinics and 2 stroke centers	Prospective cohort study,	Evaluation and tPA via real time VC	115 at community hospital versus 110 at stroke	●Rate of tPA: community hospitals 115/4727(2.4%) and Stroke centre 110/1889(5.8%), ●ICB 7.8% vs. 2.7% ($p<0.05$),

					centre	●In hospital mortality 3.5% vs. 4.5 % (NS).
Pedragosa 2009 (14)	Spain	Community hospitals >70 km away from tertiary centre.	Retrospective cohort study	Evaluation and tPA via real time VC	Total of 399 stroke patients admitted over 2 years	Significant outcomes pre vs post implementation: (Total of 399 stroke patients admitted over 2 years). ●Specialist review 17% vs. 38%, ●Inter-hospital transfers17% vs. 6%, ●Rate of tPA 4.5% vs. 9.6%, ●Time to tPA 210min vs. 162 min, ●tPA within 3 hours40% vs. 63%
Meyer 2008 (15)	USA	4 remote spoke sites	Randomised controlled study of Telemedicine vs. telephone decision making and supervision of tPA	Evaluation and tPA via real time VC or telephone. CT images were available in the telemedicine arm; Only report was available in the telephone arm.	Number of patients: 111 in telemedicine and 111 in telephone arms	●Correct decision making 98% vs. 82% ($p<0.05$), ●Rate of tPA 28% vs. 23% (NS), ●90 day FO-no difference ●90 day mortality19% vs. 13% (NS) ● ICB7% vs. 8% (NS),
Sairanen 2011 (16)	Finland	5 community hospitals 130-800 km away and one hub	Prospective cohort study,	Evaluation and tPA via real time VC	106 patients within 5 community hospitals	●At 2 years, number of patients in community hospitals: 106, ●Rate of tPA 57.5%, ●ICB 6.7%, ●3 month mortality 11.5%, ●3 month FO 49% at spoke sites vs. 58% at hub (NS).

Schwab 2007 (17)	Germany	12 Community hospitals vs. 2 stroke centres	Prospective cohort study,	Evaluation and tPA via real time VC	Over 22 months, Patient number: Community hospital 170 and stroke centre 132,	●Mortality rate at 3 months 11.2% vs. 11.5%, at 6 months 14.2% vs. 13% (NS), ●FO at 6 months 39.5% vs. 30.9 % (NS).

VC- videoconferencing, tPA-thrombolysis, ICB-intra-cerebral bleed, FTF-face to face care, FO-favourable outcome, NS-not significant

Table 3: Summary of articles describing the chemotherapy management setting, study design and outcomes

Reference	Country	Setting	Study design	Intervention at remote sites	Outcomes
Sabesan 2012 (3)	Australia	Rural town 900km away from tertiary centre	Single centre case series	Medical review and supervision of chemotherapy administration via real time VC by tertiary centre	• Number of patients receiving IVCT 83, • No inter-hospital transfers after teleoncology implementation.
Sabesan 2012(18)	Australia	Rural town 900km away from tertiary centre	Single centre case series-Questionnaire based survey of patient satisfaction	As above	• Participants 50, • 96% of patients in >80% agreement with statement "I am getting satisfactory care from the specialist on video link".

VC-videoconferencing, IVCT-intravenous chemotherapy.

Table 4: Summary of articles on telenephrology: dialysis management setting, study design and outcomes

Reference	Country	Setting	Study Design	Intervention	Participants	Results
Rygh et al 2012 (19)	USA	Patients living with home dialysis	Qualitative using semi-structured interviews	NA	N=11 patients (PD=8, HHD=3)	• Satisfied with home option • Continued to require close communication and follow up • Recognised a need for telemedicine models to increase independence.
Sicotte et al 2011 (20)	Canada	Two James Bay Cree communities- Chisasibi and Chibaugamau	Pre and post design	Tele-HD	N=19 patients (followed for 12 months pre and post)	• Health outcomes met markers from the National Kidney Foundation; pre and post. • HD sessions= 11.8 pre, 11.1 post (Chisasibi); 12.5 pre, 12.4 post (Chibaugamau) • Medication changes=8.1 pre, 3.1 post (Chisasibi);2.2 pre, 1.8 post (Chibaugamau) • Transfers to university hospitals=1.1 pre, 1.6 post (Chisasibi); 1.3 pre, 1.4 post (Chibaugamau)
Rumpsfeld 2005 (21)	Norway	University hospital of north Norway and its 2 satellite sites: Alta and Hammerfest	Prospective study	VC for daily visits and ward rounds.	9 patients followed for 8 months	• Technological (28%) and logistical (10%) problems noted • 5 hospitalisations and 1/3 of planned visiting rounds were avoided. • Economically non-viable at

						pilot level: running costs higher • Nurses reported satisfaction with technology and care provided.

NA= not applicable, HHD=home haemodialysis, PD=peritoneal dialysis, VC=Video-conference

It is apparent from viewing the tables above that telemedicine has not added to significant adverse outcomes and has safely delivered therapies such as thrombolysis, chemotherapy and dialysis to remote patients who would otherwise suffer worse health outcomes if they were unable to access these cornerstone treatments.

Discussion

The quality of most of the studies selected for this review was weak due to lack of randomised controlled trials (RCT) and small number of patients. However, given the small number of rural and remote patients and the novelty of the three fields, as well as the importance of maintaining patient autonomy around the difficult area of oncology treatments, a RCT may never be feasible in many geographically large areas. These studies have used different study designs and comparators. However, all the studies reported on similar outcomes and reported side effects, and other outcome parameters like intra-cranial bleeds, arrival time to treatment, in-hospital mortality and 3 month mortality rates were consistent across these studies. Though firm conclusions cannot be made from these studies, it seems that telestroke and teleoncology for the delivery of active interventions are feasible and safe. Furthermore, it is apparent the real time videoconferencing is preferable to telephone-based systems in terms of patient outcomes.

One limitation in implementing telestroke widely which was identified from the studies is availability of CT scanning facilities. Since most rural towns lack this, wide introduction of such models seems unlikely.

Chemotherapy administration through telemedicine is a more recent addition to the telemedicine field and thus there has not yet been significant literature on the safety and survival of these patients given the novelty of these models. However, although it is feasible to remotely supervise many toxic chemotherapy regimens via real time videoconference, the Townsville teleoncology model is suited to larger rural centers where there are resident chemotherapy-competent nurses. Therefore patients from smaller rural towns continue to travel long distances for their stroke and chemotherapy care.

To provide access to at least some part of medical therapy closer to homes, new models are required. For example, a remote chemotherapy supervision model is currently being trialed at the Townsville Cancer Centre to address this issue. In this model, selected chemotherapy regimens are administered by non chemo-competent nurses guided and supervised via real time VC by a chemo-competent nurse from TCC.

Dialysis too can be adequately provided with guidance from central renal centers. The studies looking at dialysis via VC were however scant and reported on various aspects such as economic analysis, hospital transfers and health outcomes and thus comparison and solid conclusions cannot be drawn from such one-off studies.

Within telenephrology, monitoring of rural patients on peritoneal dialysis via VC or mobile phones to address their acute complications such as infections with treatment response from urban peritoneal dialysis units has also begun. Although in one study this was complimented with n intensive home visit program, the other study used VC as a solitary trouble shooting method and monthly evaluations for their rural patients. These studies concentrated more on tele-monitoring as opposed to delivering therapies or infusions via VC. (22-24)

Gallar et al presented the results of home monitoring patients using peritoneal dialysis by installing VC equipment in their home and found this a clinically useful model for long term follow up of stable patients minimizing travel, costs and burden on patients. Medication changes were undertaken through VC and only 2% of patients required hospital presentation for management. In all cases the abdomen was successfully examined for infection or oedema in and around the catheter exit site. (25) Two other studies conducted at the same centre in the United States, first looking at health outcome and cost analysis in using nursing oversight to conduct telehealth consults with remote patients. This pilot demonstrated improved health outcomes and cost benefits. The second larger study looking at 99 patients over 3 years showed again a significant cost benefit with decrease in hospitalization and days in hospital; and reduced requirement to conduct telehealth consults with patients taking further ownership of their health. (26, 27) VC is continually being used for clinical consultation required frequently for kidney disease patients. (28)

Conclusion

Though the quality of the studies are weak, studies from all three fields report outcomes similar to standard practice and these models seem both feasible and safe to implement. Current models are suited to larger centers with adequate imaging and service capabilities. To provide equitable coverage to most rural patients, new telehealth models and more rigorous studies of their effectiveness, acceptability and safety are required.

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