Title: The efficacy of telemedicine using videoconferencing system in outpatient care for cancer patients: a systematic review and meta-analysis protocol

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Taira N is the guarantor. Uemoto Y drafted the manuscript.
All authors contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria. Kataoka Y, Wada Y developed the search strategy. Kataoka

Y, Wada Y provided statistical expertise. All authors read, provided feedback and approved the final manuscript.

Support: Funding provided by Comprehensive Support Project for Oncological Research (CSPOR).

1.Introduction

The incidence of cancer still continues to rise all over the world. Survival rates are generally increasing for most cancers due to development of health care systems to cancer[1]. As the number of cancer patients and the prognosis of cancer improve, the time and cost for outpatient care is expected to become a burden for cancer patients[2].

Telemedicine (TM) uses telecommunications technology as a tool to deliver health care to populations with limited access to care[3]. Patients and healthcare professionals can engage virtually and interactively through TM. Interactive TM has the potential to minimize the burden on patients who visit medical facilities and wait to be seen, no matter where they live. A previous systematic review (SR) has shown that interactive telemedicine can be as effective as face-to-face care in providing health care to patients with chronic diseases such as diabetes, heart failure and mental health problems[4].

The use of TM to deliver cancer care has also been a focus of attention[5]. According to previous SR, TM for cancer patients has been reported to be a convenient and reassuring method of cancer treatment that can improve QOL [6] and minimize the burden of cancer treatment and its impact on the lives of cancer patients[7]. In palliative care for cancer patients, TM using videoconferencing systems has been reported to be feasible and useful for communication between medical professionals and patients, symptom control, and clinical evaluation of patients[8]. However, these evidences are not specific to TM using video conferencing systems for outpatients with cancer, and its efficacy compared with usual face-to-face care has not been reviewed

systematically.

Therefore, further research is needed to compare the impact of interactive TM using videoconferencing systems with usual face-to-face care in the outpatient with cancer. The aim of this study is to review systematically the efficacy of interactive telemedicine using videoconferencing systems in this setting, including feasibility, satisfaction and cost.

2.Research question

P: Cancer patients at outpatient care
I: Telemedicine using videoconferencing system (Interactive telemedicine)
C: Face to face care (usual care)
O: Satisfaction, cost, proportion of attendance

3.Method

3.1 Protocol

We used a systematic review protocol template (dx.doi.org/10.17504/protocols.io.biqrkdv6). We followed the Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 for preparing this protocol[9]. We will publish this protocol in protocols.io (https://www.protocols.io/).

3.2 Inclusion criteria of the articles for the review

3.2.1 Type of studies

We will include randomized controlled trials that assess the efficacy of telemedicine using videoconferencing system in outpatient care for cancer patients provided by medical professionals. We will not apply language or country restrictions. We will include all papers including published, unpublished articles, abstract of conference and letter.
We will exclude quasi-randomization, observational and case series study. We will not exclude studies based on the observation period or publication year.

3.2.2 Study participants

Cancer patients who receive outpatient care

Inclusion criteria:
All cancer patients in outpatient care including perioperative, postoperative and metastatic setting
Any age, sex or race

Exclusion criteria:
Patients receiving telemedicine for other than cancer conditions

3.2.3 Intervention
Telemedicine using videoconferencing system in outpatient care replaced all or part of usual care
Intervention was conducted by medical professionals such as doctors, nurses and psychotherapists

3.2.4 Control
Face to face care in outpatient clinic

3.3 Type of outcomes
3.3.1 Primary outcomes
1. Satisfaction (Patient)
Definition: Patient satisfaction for outpatient care assessed by numerical rating scale (NRS)-based questionnaire
Period: During each study period

2. Cost (Money)
Definition: Average money spent on travel for outpatient visits for patients ($)
Period: During each study period

3. Outpatient attendance proportion
Definition: Proportion of attendance at planned outpatient visits, both telemedicine and face-to-face
Period: During each study period

3.3.2 Secondary outcomes
1. Satisfaction (Medical professional)
Definition: Medical professional satisfaction for outpatient care assessed by NRS-based questionnaire
Period: During each study period

2. Cost (Time)
Definition: Average time spent on travel for outpatient visits (minutes)
Period: During each study period

3. Time devoted to outpatient care
Definition: Average time spent on outpatient care (minutes)
Period: During each study period

4. Patient wait time
Definition: Average time spent on waiting for outpatient care (minutes)
Period: During each study period

5. Depression score
Definition: Depression score measured by any validated questionnaire, such as HAM-D and IDS-C
Period: At the end of the study

6. Intensity of cancer pain
Definition: Intensity of cancer pain as assessed by Brief Pain Inventory
Period: At the end of the study

3. All adverse events
Definition: definition of adverse events is set by original authors or the proportion of unexpected hospitalization due to delayed outpatient care.
Incidence proportion of all adverse events
Period: during follow up period

3.4 Search method
3.4.1 Electronic search
We will search the following databases:
1. the Cochrane Central Register of Controlled Trials (CENTRAL);
2. MEDLINE via PubMed;
3. EMBASE via Dialog;
5. CINAHL;
See Appendix 1, 2, and 3 for the search strategies.

3.4.2 Other resources
We will also search the following databases for ongoing or unpublished trials:
1. the World Health Organization International Clinical Trials Platform Search Portal (ICTRP);

2. ClinicalTrials.gov;

See Appendix 4, 5 for the search strategies.

We will check the reference lists of studies, including international guidelines as well as the reference lists of eligible studies and articles citing eligible studies. We will ask the authors of original studies for unpublished or additional data.

3.5 Data collection and analysis

3.5.1 Selection of the studies

Two independent reviewers (Uemoto Y, Yamanaka T) will screen titles and abstracts, followed by the assessment of the eligibility based on the full texts. We will contact original authors if relevant data is missing. Disagreements between the two reviewers will be resolved by discussion, and if this fails, a third reviewer will act as an arbiter (Kikawa Y, Kataoka Y and Wada Y).

3.5.2 Data extraction and management

Two reviewers (Uemoto Y, Yamanaka T) will perform independent data extraction of the included studies using standardized data collection form. We will use a pre-checked form using 10 randomly selected studies.

The form will include the information on study design, study population, interventions and outcomes. Any disagreements will be resolved by discussion, and if this fails, a third reviewer will act as an arbiter (Kikawa Y, Kataoka Y and Wada Y).

3.6 Assessment of risk of bias in included studies

Two reviewers (Uemoto Y, Yamanaka T) will evaluate the risk of bias independently using the Risk of Bias 2[10]. Disagreements between the two reviewers will be discussed, and if this fails, a third reviewer (Kikawa Y, Kataoka Y and Wada Y) will be acting as an arbiter, if necessary.

3.7 Measures of treatment effects

We will pool the mean differences and the 95% CIs for the following continuous variables: Patient and medical professional satisfaction, cost of money and time, outpatient attendance proportion, time devoted to outpatient care, patient wait time, depression score and intensity of cancer pain.

If several different scales have been used in the included studies, we will pool the effect estimates using standard mean differences (SMDs)

We will summarize adverse events based on the definition by the original article, but we will not perform meta-analysis.

3.8 Unit of analysis issues

Clustering at the level of the enrolled units in cluster randomized studies

In dealing with cluster-RCTs, for continuous data, only the sample size will be reduced; means and standard deviation will remain unchanged.[3]

Randomized cross-over studies

We will consider only data from the first period.

Multiple comparisons

All intervention groups that are relevant to this review will be included.

3.9 Handling of missing data

We will ask not-presented data to the original authors.

3.9.1 Missing outcomes

For continuous data, we will not impute missing data based on the recommendation by Cochrane handbook[11]. We will perform meta-analysis about the available data in the original study.

3.9.2 Missing statistics

When original studies only report standard error or p-value, we will calculate the standard deviation based on the method by Altman[12]. If we don't know these values when we contact the authors, standard deviation will be calculated by confidence interval and t-value based on the method by Cochrane handbook[11], or validated method[12]. Validity of these methods will be analyzed by sensitivity analysis.

3.10 Assessment of heterogeneity

We will evaluate the statistical heterogeneity by visual inspection of the forest plots and calculating the I2 statistic (I2 values of 0% to 40%: might not be important; 30%to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; 75% to 100%: considerable heterogeneity). When there is substantial heterogeneity (I2> 50%), we will assess the reason of the heterogeneity. Cochrane Chi2test (Q-test) will be performed for I2 statistic, and P value less than 0.10 will be defined as statistically significant.

3.11 Assessment of reporting bias

We will search the clinical trial registry system (ClinicalTrials.gov and ICTRP) and will perform extensive literature search for unpublished trials. To assess outcome reporting bias, we will

compare the outcomes defined in trial protocols with the outcomes reported in the publications. We will assess the potential publication bias by visual inspection of the funnel plot. We will conduct Egger test to assess the publication bias. We will not conduct the test when we find less than 10 trials or trials which have similar sample size.

3.12 Meta-analysis

Meta-analysis will be performed using Review Manager software (RevMan 5.4.1). We will use a random-effects model.

3.13 Subgroup analysis

To elucidate the influence of effect modifiers on results, we will evaluate the subgroup analyses of the primary outcomes on the following factors when sufficient data are available.

- 1. (For participants) type of cancer, living in rural or urban area
- 2. (For intervention) telemedicine with video conferencing system with or without any application

3.14 Sensitivity analysis

We will undertake the following sensitivity analyses for the primary outcomes to assess whether the results of the review are robust to the decisions made during the review process.

1. Exclusion of studies using imputed statistics.

2. Missing participants: verify the robustness of the results by seeking informative missingness odds ratios[13].

3. Only the participants who complete the study with complete data

4. Summary of findings table

Two reviewers (Uemoto Y, Wada Y) will evaluate the certainty of evidence based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach[14]. Disagreements between the two reviewers will be discussed, and if this fails, a third reviewer (Kikawa Y and Kataoka Y) will be acting as an arbiter, if necessary.

Summary of findings table will be made for the following outcome based on the Cochrane handbook[11].

Patient satisfaction, cost of money, outpatient attendance rate, medical professional satisfaction, time devoted to outpatient care, patient wait time and intensity of cancer pain.

5. Conflict of Interest

The authors declare no conflicts of interests.

6. Support
Funding provided by Comprehensive Support Project for Oncological Research (CSPOR).

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of findings tables. *Journal of Clinical Epidemiology* **64**, 383–394 (2011).

Appendix 1: MEDLINE (PubMed) search strategy

#1 neoplasms [Mesh] OR neoplasms [tiab] OR carcinoma [tiab] OR cancer [tiab] OR tumor [tiab] OR malignan*[tiab]

#2 telemedicine [Mesh] OR videoconferencing [Mesh] OR telemedicine [tiab] OR videoconferencing [tiab] OR “remote consultation” [tiab] OR telehealth [tiab] OR mhealth [tiab] OR ehealth [tiab] OR “mobile health” [tiab]

#3 randomized controlled trial [pt]

#4 controlled clinical trial [pt]

#5 randomized [tiab]

#6 placebo [tiab]

#7 drug therapy[sh]

#8 randomly [tiab]

#9 trial [tiab]

#10 groups [tiab]

#11 #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

#12 animals [mh] NOT humans [mh]

#13 #11 NOT #12

#14 #1 AND #2 AND #13

Appendix 2: CENTRAL search strategy

(((((([mh neoplasms]) OR (neoplasms:ti,ab)) OR (cancer:ti,ab)) OR (tumor:ti,ab)) OR (carcinoma:ti,ab)) OR (Malignan*:ti,ab)) AND (((((((([mh telemedicine]) OR ([mh videoconferencing])) OR (telemedicine:ti,ab)) OR (videoconferencing:ti,ab)) OR (telehealth:ti,ab)) OR (mhealth:ti,ab)) OR (ehealth:ti,ab)) OR ("mobile health":ti,ab)) OR ("remote consultation":ti,ab))

Appendix 3: EMBASE (Dialog) search strategy

S1 EMB.EXACT.EXPLODE(neoplasm) OR ab(neoplasms) OR ti(neoplasms) ab(cancer) OR ti(cancer) OR ab(tumor) OR ti(tumor) OR ab(malignan*) OR ti(malignan*)OR ab(carcinoma) OR ti(carcinoma

S2 EMB.EXACT.EXPLODE("telemedicine") OR EMB.EXACT.EXPLODE("videoconferencing") OR ab(telemedicine) OR ti(telemedicine) OR ab(videoconferencing) OR ti(videoconferencing) OR ab(telehealth) OR ti(telehealth) OR

ab(mhealth) OR ti(mhealth) OR ab(ehealth) OR ti(ehealth) OR ab(“mobile health”) OR ti(“mobile health”) OR ab("remote consultation") OR ti("remote consultation")
S3 S1 AND S2
S4 (EMB.EXACT("double blind procedure")) OR (ab(double NEAR/1 blind*) OR ti(double NEAR/1 blind*)) OR (ab(placebo*) OR ti(placebo*)) OR (ab(blind*) OR ti(blind*))
S5 S3 AND S4

Appendix 4: CINAHL search strategy
(((((((MH "neoplasms+")) OR ((TI neoplasms OR AB neoplasms))) OR ((TI cancer OR AB cancer))) OR ((TI tumor OR AB tumor))) OR ((TI carcinoma OR AB carcinoma))) OR ((TI Malignan* OR AB Malignan*))) AND ((((((((((MH "telemedicine+")) OR ((MH "videoconferencing+"))) OR ((TI telemedicine OR AB telemedicine))) OR ((TI videoconferencing OR AB videoconferencing))) OR ((TI telehealth OR AB telehealth))) OR ((TI mhealth OR AB mhealth))) OR ((TI ehealth OR AB ehealth))) OR ((TI "mobile health" OR AB "mobile health"))) OR ((TI "remote consultation" OR AB "remote consultation")))) AND (((MM“Randomized Controlled Trials”) OR (MM“Random Assignment”) OR (MH“Prospective Studies”) OR (MH“Multicenter Studies”) OR (MH “Double-Blind Studies”) OR (MH “Single-Blind Studies”) OR (MH “Triple-Blind Studies”) OR (MH “Placebos”)) OR (random* OR (controlled AND (stud* or trial*)) OR ((blind* or mask*) AND (single or double or triple))))

Appendix 5: ICTRP search strategy
Condition or disease: neoplasms OR tumor OR carcinoma OR malignan*
Intervention: telemedicine OR videoconferencing OR telehealth OR mhealth OR ehealth OR "mobile health" OR "remote consultation"

Appendix 6: ClinicalTrials.gov search strategy
Condition or disease: neoplasms OR tumor OR carcinoma OR malignan*
Intervention: telemedicine OR videoconferencing OR telehealth OR mhealth OR ehealth OR "mobile health" OR "remote consultation"