Prospective Pilot Study of Telehealth as Domiciliary Follow-up after Hematopoietic Cell Transplantation during the COVID19 Pandemic

Alberto Mussetti, Maria Queralt Salas, Maria Condom, Maite Antonio, Cristian Ochoa, Iulia Ivan, David Jimenez Ruiz-De la Torre, Gabriela Sanz Linares, Belen Ansoleaga, Beatriz Patinño-Gutierrez, Laura Jimenez-Prat, Rocio Parody, Ana Sureda-Balari

Submitted to: JMIR Formative Research
on: November 28, 2020

Table of Contents

Prospective Pilot Study of Telehealth as Domiciliary Follow-up after Hematopoietic Cell Transplantation during the COVID19 Pandemic

Alberto Mussetti[1, 2] MD; Maria Queralt Salas[1, 2] MD; Maria Condom[1, 2] MD; Maite Antonio[2, 3] MD; Cristian Ochoa[2, 4, 5] DPhil; Iulia Ivan[1, 2] MD; David Jimenez Ruiz-De la Torre[1, 2] MD; Gabriela Sanz Linares[1, 2] MD; Belen Ansoleaga[1, 2] MD; Beatriz Patinño-Gutierrez[1]; Laura Jimenez-Prat[1]; Rocio Parody[1, 2] MD; Ana Sureda-Balari[1, 2] MD

[1]Clinical Hematology Department, Institut Català d'Oncologia-Hospitalet, Barcelona, Spain L'Hospitalet de Llobregat, Barcelona ES
[2]Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), Barcelona ES
[3]Oncohematogeriatrics Unit, Institut Català d'Oncologia-Hospitalet Barcelona ES
[4]Institut Català d'Oncologia, Psycho-Oncology Unit and ICOnnecta't Health Program, Hospital Duran i Reynals, L'Hospitalet de Llobregat Barcelona ES
[5]Clinical Psychology and Psychobiology Department, Faculty of Psychology Barcelona ES

Corresponding Author:
Alberto Mussetti MD
Clinical Hematology Department, Institut Català d'Oncologia-Hospitalet, Barcelona, Spain
Hospital Duran i Reynals, Avinguda de la Gran Via de l'Hospitalet, 199-203,
L'Hospitalet de Llobregat, Barcelona
ES

Abstract

Patients receiving hematopoietic cell transplantation are at increased risk of infectious complications. A higher mortality was shown for these patients affected by COVID19. In this prospective study, we developed and tested a telemedicine platform to improve the domiciliary follow-up of patients who had received a transplant. Daily monitoring of vital signs, symptoms and psychological status was performed through a mobile phone application and clinically validated medical devices. Sixteen patients were enrolled for this proof-of-concept study. Thirty-eight percent of transplants were autologous and sixty-two percent were allogeneic. Four patients were not able to use the app due to their inability in using smartphone applications. Patients' adherence in reporting study data was acceptable. The subjective perception of the study was considered positive from the majority of patients. We showed how to implement a specific telemedicine platform in the setting of transplanted patients with promising results.

(JMIR Preprints 28/11/2020:26121)
DOI: https://doi.org/10.2196/preprints.26121

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Prospective Pilot Study of Telehealth as Domiciliary Follow-up after Hematopoietic Cell Transplantation during the COVID19 Pandemic

Mussetti A[1,2], Salas MQ[1,2], Condom M[1,2], Antonio M[2,3], Ochoa C[2,4,5], Ferro García T, Ivan I[1,2], Jimenez Ruiz-de la Torre D[1,2] , Sanz G[1,2], Ansoleaga B[1,2], Patiño Gutierrez B[1], Parody R[1,2], Sureda A[1,2,6].

1)Clinical Hematology Department, Institut Català d'Oncologia-Hospitalet, Barcelona, Spain

2)Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), Barcelona, Spain

3)Oncohematogeriatrics Unit, Institut Català d'Oncologia-Hospitalet, Barcelona, Spain

4) Institut Català d'Oncologia, Psycho-Oncology Unit and ICOnnecta't Health Program, Hospital Duran i Reynals, L'Hospitalet de Llobregat, Barcelona, Spain.

5) Clinical Psychology and Psychobiology Department, Faculty of Psychology, Universitat de Barcelona, Spain.

6)Universitat de Barcelona, Barcelona, Spain

Text word count = 1235

Number of figures = 0

Number of tables = 1

Number of references = max 6

Running title: Telehealth post HCT during COVID19 pandemic

Corresponding author: Mussetti A, amussetti@iconcologia.net

Key Words: SARS-COV2, CoVID19, Hematology, Hematopoietic Cell Transplantation, Telemedicine

Abstract

Background: Patients who have recently received hematopoietic cell transplant (HCT) are at higher

risk of acute complications in the first weeks after discharge, especially during the COVID19 pandemic.

Objective: the aim of this study was to test the use of a telehealth platform for the follow-up of transplanted patients during the first 2 weeks from discharge.

Methods: 21 patients who received autologous or allogeneic HCT for hematological malignancies were screened from the 30th April 2020 to 15th July 2020. The telehealth platform consisted in the daily collection of vital signs and physical or psychological symptoms for 2 weeks after hospital discharge. Required medical devices (oximeter, blood pressure monitor)were given to patients and a dedicated smartphone application was developed to collect this data. Daily medical revision of the data was performed form a hematologist specialized in HCT through a web-based software.

Results: Only 12 out of 21 patients were able to enter or complete the study. Technological barriers were the most frequent limiting factor of the study. In the 12 patients who completed the study, adherence in reporting data was high. Patients' experience in using such a system was considered generally good. In 2 cases, the system allowed the early recognition of acute complications.

Conclusion: this pilot study showed that application of telehealth systems can be applied in the early post-transplant setting with evident advantage for the physicians and patients in terms of both medical and psychological perspectives. Technological issues still represent a problem in the applicability of such a system, especially for elderly patients. Easier to use technologies could help in the future in expanding the use of telehealth systems in this setting.

Patients receiving hematopoietic cell transplant (HCT) have a high risk of developing severe acute toxicities in the early post-transplant period. An increased mortality risk has been observed in transplanted patients affected by Coronavirus Disease 2019 (COVID19) with an estimated mortality rate between 20-40%.(1,2) While other hematological procedures can be postponed in case of emergency, there is an international agreement in not deferring transplant procedures, especially for rapidly progressing diseases such as acute leukemias and aggressive lymphomas. Because of this, it

is necessary to 1) improve the domiciliary clinical monitoring of transplanted patients in order to rapidly detect clinical deterioration and 2) to reduce unnecessary in-person visits that might increase the risk of intra-hospital contagion. During the last few years, the development of smart devices to assess vital signs or physical activity has emerged as breakthrough innovations in the oncological setting.(3–5) Digital technologies allow us to perform real-time monitoring of patients' clinical status. In COVID19 patients, the use of devices such as digital oximeters allow early detection of clinical deterioration and guarantee a safer domiciliary follow-up. This is of paramount importance for transplanted patients, characterized by higher COVID19-related mortality.
The aim of this study is to report the feasibility of a real-time patient monitoring system through the use of a smartphone application and mobile healthcare devices (SMARTCOVID19 study). The institutional review board approved the study. Inclusion criteria were: age ≥ 18 years, having received autologous or allogeneic HCT during the hospitalization, having a smartphone with an operating system able to support the SMARTCOVID19 application. Exclusion criteria were: absence of an adequate social support.
Patient education regarding the use of the platform was made from a hematologist at time of enrollment, 1 or 2 days before hospital discharge.

Vital signs (cardiac frequency, oxygen saturation, and arterial blood pressure) were collected daily through the use of clinically validated oxymeters (Onyx II®, Nonin Inc, Plymouth MN USA) and blood pressure monitor (iHealth Track®, Mountain View, CA USA) while temperature was measured through domiciliary thermometers. Patients were educated to measure their respiratory frequency. A checklist of clinical symptoms was filled daily (presence of cough, myalgia, headache, fatigue, dyspnea, emesis, odynophagia, rhinitis, conjunctivitis, chest pain). An analog visual scale "thermometer" (0-10) to detect potential cases of anxiety or depressive disorders was reported daily. Scores of ≥6 were automatically transmitted through the platform to a referral psycho-oncologist which eventually contacted the patients and evaluate the need of a psychological support through

videoconference. A chat service was available for non-urgent communications. All the data were reported to an online platform (www.saludencasa.trilema.es) through a smartphone application compatible with Apple and Android systems (iOS v.9 or Android v.6 or more recent versions, “Saludencasa”, Fundación Trilema, Valencia, Spain). A hematologist with experience in HCT revised all patients’ data daily. Programmed alarms were set in case of any of the following situations: fever ≥38 ºC, oxygen saturation ≤92%, tachycardia ≥125/bpm, hypotension (systolic<90 mmHg, diastolic > 60 mmHg), altered mental status, persistent emesis or diarrhea (lasting more than 48 hours).In case of alarm activation, a first phone contact was made by the hematologist which evaluate the need for an in-person visit and the clinical management which was considered most appropriate. The outpatient monitoring started from the day of hospital discharge ±2 days and continued for 14 days. Study accrual period started from the 30th April 2020 to 15th July 2020. Data were collected prospectively and all patients signed informed consent. After two weeks from the end of the recruitment period, patients were contacted by phone and asked to reply a satisfaction questionnaire.

During the study period, 16 out of 21 transplanted patients were successfully recruited into the study (80% feasibility). Reasons for not being enrolled were: language incompatibility (1 patient), no consent (1 patient) and no compatible smartphone (3 patients). Of the 16 enrolled patients, median age was 50 (range 22-70 years), 37% were female and 94% had lymphoid diseases. Thirty-eight percent of HCTs were autologous and 62% were allogeneic.

Of the 16 enrolled patients, 4 were not able to use the app due to inability in using smartphone applications. Of the remaining 12 patients, adherence in reporting study data (number of days reported of the planned 14 days study period) was as follows (average): temperature 89%, oxygen saturation 90%, respiratory frequency 70%, cardiac frequency 85%, blood pressure 89%, symptoms reporting 65%, emotional distress 71%.

Automatic alarms were activated only 3 times: twice for the presence of clinical symptoms and once for emotional distress. A videoconference with the psycho-oncologist was used by only one patient.

The chat service to communicate with hospital personnel was used in 4 patients. Despite the feasibility nature of the study, data collected with the digital system helped the clinician to early recognize calcineurin-inhibitors related arterial hypertension (1 patient) and acute cutaneous graft-versus-host disease grade I (1 patient).
Only two patients of the whole cohort were readmitted within 14 days from discharge due to grade 4 odynophagia related to HSV1/2 reactivation.
Patients' experience with telehealth systems are reported in **table 1**.

Our prospective study showed that implementation of mobile healthcare devices and use of smartphone applications for self-reported outcomes is feasible in the post HCT setting. In a study conducted by Nawas et al., it was shown how telehealth evaluations could be useful also in the early peri-transplant period with a high satisfaction rate from the patients' point of view.(6) Also in our study, patients felt safer when using the telehealth system. However, only a few patients would completely substitute an in-person visit with a complete telehealth monitoring. This suggests how an in-person visit with a medical doctor is still considered the preferred follow-up modality for transplanted patients. Apart from vital signs monitoring and blood tests results, which could be evaluated without the presence of the patient, other factors cannot be replaced by telehealth. Human contact and empathy are still largely needed during a visit. From a feasibility and adherence point of view, two observations emerge from our study. The first one is that only 57% of potential patients finally used the telehealth system. Technological barriers such as incompatible smartphones or inexperience in using smartphone applications were the main causes for study failure. This problem was more frequently observed in elderly patients living alone or without caregivers able to help them in using the devices. A solution to this could be to automatize data collection through the use of automatic devices. Newer wearable devices could allow real-time monitoring of patients cardiac frequency, oxygen saturation and physical activity in an automated manner. The second

technological issue was encountered in those people who finally succeed in using the platform. Also in this case, adherence to report clinical parameters such as respiratory frequency or symptoms was low. The use of current wearable devices could also resolve this adherence issue. Possibly, also psychological barriers could have contributed in reducing study adherence apart from technical issues. A better patient education in terms of technology utilization could also improve this point, and should always be considered when applying digital medicine. Finally, the quality of the telehealth monitoring should be complemented and improved by the collection of other clinically relevant parameters. For example, a virtual physical examination could be made through the use of high-quality video calls, digital stethoscopes and weight scales.(6,7) In our study, the system worked well in detecting acute complications such as infections, dehydration. It is adapt for the monitoring of the early post-transplant period where acute complications are more frequent. For the long term follow-up, it should be implemented with other technologies, for example to improve the visual communication between physicians and patients.
Study limitations were represented from the small number of patients. However, the study population was considered sufficient for a pilot study. In fact, the results obtained should be used to improve the creation of the next study which will accrual a larger number of patients. Also, the use of newer technologies could be influenced from the country or the hospital resources. It is possible that such a system could not be implemented if the hospital or the health care system cannot afford such expenses. This applicability issue is common to the majority of studies using newer technologies.

In conclusion, telehealth monitoring could potentially improve patient's follow-up in terms of both physical and psychological outcomes. This is especially true whenever an external cause could impede in-person visits, such COVID19 pandemic. Technological problems still represent a barrier to a wider application of telehealth monitoring systems in the medical setting and should be considered for future studies.

Author contributions:

Conception and design: A.M.

Financial support: none

Collection and assembly of data: All authors.

Data analysis: A.M.

Interpretation: All authors.

Manuscript writing: First draft prepared by A.M. All authors helped in revising the manuscript.

Final approval of manuscript: All authors

Disclosure of conflict of interest: The authors have declared no relevant conflicts of interest related to this study

Aknowledgements

All patients and their families.

All the health care workers and scientists helping our society against the SARS-COV2 outbreak.

Bibliography

1. Shah GL, DeWolf S, Lee YJ, Tamari R, Dahi PB, Lavery JA, et al. Favorable outcomes of COVID-19 in recipients of hematopoietic cell transplantation. J Clin Invest [Internet]. 2020 Sep 8 [cited 2020 Oct 4]; Available from: http://www.jci.org/articles/view/141777

2. Passamonti F, Cattaneo C, Arcaini L, Bruna R, Cavo M, Merli F, et al. Clinical characteristics and risk factors associated with COVID-19 severity in patients with haematological malignancies in Italy: a retrospective, multicentre, cohort study. Lancet Haematol. 2020 Oct;7(10):e737–45.

3. Patel M, Cooney MM, Caimi PF, Randall RE, Metheny LL, Mendiratta P, et al. Pilot study for the use of wearable devices for patients undergoing oral chemotherapy. J Clin Oncol. 2020 May 20;38(15_suppl):e14103–e14103.

4. Liao Y, Thompson C, Peterson S, Mandrola J, Beg MS. The Future of Wearable Technologies and Remote Monitoring in Health Care. Am Soc Clin Oncol Educ Book. 2019 May;(39):115–21.

5. Cox SM, Lane A, Volchenboum SL. Use of Wearable, Mobile, and Sensor Technology in Cancer Clinical Trials. JCO Clin Cancer Inform. 2018 Dec;(2):1–11.

6. Nawas MT, Landau HJ, Sauter CS, Featherstone CA, Kenny SA, Rodriguez ES, et al. Pilot Study of Telehealth Evaluations in Patients Undergoing Hematopoietic Cell Transplantation. Biol Blood Marrow Transplant. 2020 Jun;26(6):e135–7.

7. Lupo-Stanghellini MT, Messina C, Marktel S, Carrabba MG, Peccatori J, Corti C, et al. Following-up allogeneic transplantation recipients during the COVID-19 pandemic. Lancet Haematol. 2020 Aug;7(8):e564–5.

Question	**Mean Score (#patients = 12)** **(1 to 5 score; 1 = disagree, 5 = agree)**
Overall satisfaction with the telehealth system	4.67
Did you feel safer at home with the use of Telehealth System?	4.67
Did you think that using such a device has improved your domiciliary follow up?	4.67
Was the application easy to use?	4.50
When you feel well, would you be comfortable in changing in-person visit with telemedicine?	3.50

Table 1 Patients experience with the telehealth system.