

Original Research

Cite this article: Beypinar I. After an earthquake: The comparison of psychological status of resident and earthquake survivor cancer patients. *Disaster Med Public Health Prep.* 18(e54), 1–4. doi: <https://doi.org/10.1017/dmp.2024.62>.

Keywords: earthquake; cancer; depression; anxiety; stress; disaster

Corresponding author: Ismail Beypinar; Email: ibeypinar@yahoo.com.

After an Earthquake: The Comparison of Psychological Status of Resident and Earthquake Survivor Cancer Patients

Ismail Beypinar MD 

Department of Medical Oncology, Alanya Alaaddin Keykubat University, Alanya, Turkey

Abstract

Objective: Natural disasters such as earthquakes can have a significant impact on cancer treatment and care. The objective of the study was to evaluate the psychological effect of the earthquake on survivor cancer patients compared to regular cancer patients.

Methods: Cancer patients who were evacuated from earthquake sites and referred for the continuation of their treatment, as well as regular resident patients were included in the study. The resident cancer patients were compared with the study population as a control group. DASS-21 forms were filled based on patients' declarations.

Results: Forty-six patients were earthquake survivors and 55 were resident cancer patients. Stress scores were significantly higher in earthquake survivors ($P = 0.021$). In contrast, there was no difference in stratified groups due to DASS-21 categorization in stress scores while depression and anxiety subgroups had significant differences ($P = 0.012$; $P < 0.001$). Also, women significantly had a worse outcome in the depression and anxiety categories ($P = 0.028$; $P = 0.021$) while no difference was observed in men.

Conclusion: Recent earthquakes in Turkey had psychological negative effects on oncology patients. The increased stress, depression, and anxiety levels were observed in earthquake survivors who were evacuated from the disaster zone and compared to the control group.

Background

Cancer is a major health concern worldwide, affecting millions of people each year. Cancer treatment typically involves a combination of surgery, radiation therapy, and chemotherapy. However, natural disasters such as earthquakes can have a significant impact on cancer treatment and care.¹

In some disasters such as nuclear disasters, earthquakes, hurricanes, and floods, increased movement of people may occur, which may result in loss of contact with family, and friends, as well as relatives; this can result in difficulties in retrieving medical information of patients. Also, there may be social isolation and traffic restrictions in times of these incidences such as pandemics.^{2–5} Two earthquakes which struck Eastern Turkey resulted in a humanitarian tragedy on February 6 and 20, 2023. Seventeen cities were affected by over 50 000 deaths and 100 000 injuries occurred. After the destruction of 345 000 buildings, more than 2 million survivors were evacuated to nearby cities, such as Antalya, and Konya, as well as Mersin, and Niğde.⁶ The International Organization for Migration has speculated that nearly 3 million people need new homes.^{6,7} Ten state and university hospitals with high oncologic treatment capacity were destroyed or out of order after the earthquake.⁸

During the great earthquake in 2011 in Japan, medical facilities provided immediate treatments for disaster survivors. Facility destruction, as well as loss of medical information, may have additional effects on cancer treatment. In addition to this phenomenon, after the restoration of the facilities, lifelines, and transportation, the life of cancer patients significantly changed compared to pre-disaster time.^{9,10} Cancer patients need a good life balance to control adverse events, cancer-related symptoms, and drug availability.¹¹

Traumatic events have negative effects on psychology such as depression, anxiety, and post-traumatic stress disorder.^{12,13} The intervention on patients' psychosociology may improve the quality of life and decrease the symptoms of depression and anxiety.^{14,15} Hospital Anxiety and Depression Scale (HADS) is used to measure the depression and anxiety levels of the patient; affecting their quality of life while suffering from cancer.¹⁶ Prior studies showed 10 - 50% of cancer patients suffer from psychosocial disorders such as social isolation, despair, anxiety, and depression which worsen with the stage of cancer.¹⁷ Depression was shown to harm treatment outcomes and quality of life in cancer patients. Also, anxiety is frequently accompanied by cancer, resulting in psychological symptoms. Although ineffective coping strategies result in increased depression and anxiety, patients with high social support have decreased levels of depression and anxiety.^{18–20}

The objective of the study was to evaluate the psychological effect of the earthquake on cancer patients who moved from disaster zones and compare with resident cancer patients who are not affected from the disaster.

Methods

Study Population

The study is based on the records of patients' who were referred to Alanya Alaaddin Keykubat University, Department of Medical Oncology, for treatment after February 6, 2023. Alanya city center is in the eastern part of Antalya province, 600 km away from the disaster zone and was not affected by the earthquakes. Fifty thousand earthquake survivors from Hatay and İskenderun, including cancer patients were evacuated via sea route and placed in the hotels in Alanya. Cancer patients who were evacuated from earthquake sites and referred for the continuation of their treatment and resident cancer patients who live in Alanya were included in the study. The resident cancer patients were compared with the study population as the control group. The patients who were treated between February 6 and March 17, 2023, were matched. The earthquake survivor cancer patients were relocated to other cities after March 17, 2023. Patients' (study and control group) demographics status, diagnosis, stages, and ongoing treatments were recorded.

Psychological Evaluation

DASS-21 evaluation forms were filled based on patients' declarations. DASS-21 is a form-based scale evaluating depression anxiety and stress. Each category has 7 questions, and each answer has points between 0 and 3. Higher points indicate worse outcomes. Cumulative points were translated into categories for each group for depression, anxiety, and stress: normal, mild, moderate, and severe, as well as very severe. The Turkish version of DASS-21 is translated and validated in prior studies.²¹ The questionnaire form is available in the appendix.

Ethics

The study was approved by the local ethics committee of Alanya Alaaddin Keykubat University, and the trial was conducted in accordance with the Declaration of Helsinki's Principles (Ethic committee decision date and number is March 22, 2023 and 5-07 respectively).

Statistics

The statistical analysis of the study was performed with SPSS software (Statistical Package for the Social Sciences, version 22.0; SPSS Inc., Chicago, IL, USA) and E-PICOS. The Kolmogorov-Smirnov test was used to determine whether data conformed to a normal distribution. Descriptive data was presented as either means or median for continuous variables, and frequencies and percentages are reported for categorical variables. Z-test was performed to confirm the difference in the Chi-square test.

Results

Forty-six patients were earthquake survivors and 55 were regular patients. There was no significant difference between earthquake survivor cancer patients and the control group in terms of age, gender, diagnosis, and marital or educational status. The groups

Table 1. The comparable features of the patient and control group

Features	Earthquake Survivors	Control Group	P - value
Age	Mean ± SD	Mean ± SD	0.77
	59.3 ± 11.7	54.4 ± 12.7	
Gender	n (%)	n (%)	0.78
Female	28 (60.9)	32 (58.2)	
Male	18 (39.1)	23 (41.8)	
Marital Status	n (%)	n (%)	0.84
Single	11 (23.9)	12 (22.2)	
Married	35 (76.1)	42 (77.8)	
Education Status	n (%)	n (%)	0.24
Illiterate	6 (13.0)	3 (5.6)	
Primary School	24 (52.2)	23 (42.6)	
Mid Education	8 (17.4)	17 (31.5)	
University	8 (17.4)	11 (20.4)	
Diagnosis	n (%)	n (%)	0.30
Breast	14 (30.4)	15 (27.3)	
Colorectal	4 (8.7)	8 (14.5)	
Lung	2 (4.3)	6 (10.9)	
Non-colon GIS	4 (8.7)	7 (12.7)	
Genitourinary	6 (13.0)	1 (1.8)	
Gynecology	7 (15.2)	8 (14.5)	
Other	9 (19.6)	10 (18.2)	
Stage	n (%)	n (%)	0.007
I	2 (5.0)	0 (0.0)	
II	14 (35.0) a	6 (12.0) b	
III	6 (15.0) a	19 (38.0) b	
IV	18 (45.0)	25 (50.0)	
Ongoing Chemotherapy	n (%)	n (%)	0.005
Yes	33 (71.7)	51 (92.7)	

a/b: Statistically significant subgroups.

showed significant difference in stage and ongoing treatment. The comparable information of the study population was demonstrated in Table 1.

There was no difference observed in the anxiety and depression scores of both groups. Stress scores had significant differences between groups which was higher in earthquake survivors. ($P = 0.021$) In contrast, there was no difference in stratified groups due to DASS-21 categorization in stress scores while depression and anxiety subgroups had significant differences. More earthquake survivor cancer patients had severe anxiety and depression compared to resident cancer patients. ($P = 0.012$; $P < 0.001$) Also, women significantly had a worse outcome in the depression and anxiety categories ($P = 0.028$; $P = 0.021$) while no difference was observed in men. The comparable difference is described in Table 2.

Limitations

The study was performed at the acute onset of the earthquake and had a limited study population. Information on the social status of the study population was absent such as social support, monthly income, loss of family during the earthquake, and receiving psychological support. Also, the long-standing psychological effect

Table 2. The comparable difference in depression, anxiety, and stress between groups

Features	Earthquake Survivor	Control Group	P - value
Stress Score	6.8 ± 4.8 [¶]	4.7 ± 3.9 [¶]	0.021
Anxiety Score	5 (0 - 19) [¶]	3 (0 - 16) [¶]	0.13
Depression Score	6 (0 - 17) [¶]	3 (0 - 13) [¶]	0.16
Stress Category	n (%)	n (%)	0.32
Normal	28 (60.9)	42 (76.4)	
Mild	6 (13.0)	6 (10.9)	
Moderate	5 (10.9)	4 (7.3)	
Severe	5 (10.9)	3 (5.5)	
Extremely Severe	2 (4.3)	0 (0.0)	
Anxiety Category	n (%)	n (%)	0.062*
Normal	19 (41.3)	32 (58.2)	
Mild	8 (17.4)	9 (16.4)	
Moderate	4 (8.7)	3 (5.5)	
Severe	4 (8.7)	8 (14.5)	
Extremely Severe	11 (23.9) a	3 (5.5) b	<0.001
Depression Category	n (%)	n (%)	0.09*
Normal	22 (47.8)	35 (63.6)	
Mild	4 (8.7)	6 (10.9)	
Moderate	11 (23.9)	9 (16.4)	
Severe	4 (8.7)	5 (9.1)	
Extremely Severe	5 (10.9) a	0 (0.0) b	0.012

[¶]Mean with standard deviation;

[¶]median with minimum and maximum values;

*statistically significant subgroup in test;

a/b: statistically significant subgroups.

of destruction may not be seen in the acute phase of the disaster. Our study did not evaluate the partners' status due to the acute onset of the disaster. Also, the prior psychological diseases and treatment per patient were not evaluated which decreased the value of the information gathered.

Discussion

To our knowledge, this is the first study evaluating the psychological effect of earthquakes on cancer patients. Although the psychological problems such as depression, anxiety, and stress have been extensively studied, there is a paucity of literature examining the effects of natural disasters on this patient group.²²

The hazardous effects of natural disasters are determined by the number of individuals impacted and their vulnerability status, with insufficiency being a key factor.²³ In terms of natural disasters, the social community collapses, and especially vulnerable people such as cancer patients are affected more compared with the other parts of the population.²⁴ Patients with chronic conditions such as diabetes, respiratory diseases, cancer, and cardiovascular diseases are the most vulnerable patient groups during natural or man-made disasters.^{25,26} In a meta-analysis, it was observed that natural disasters have negative effects on cancer care, and it is advised to have special precautions for oncology patient care and infrastructure.¹ In a large meta-analysis mainly investigating the Wenchuan earthquake, prior illness was shown to be a risk factor for post-disaster depression in both adults and children.²⁷ There is limited data reporting the negative effect of earthquakes on cancer

care in Turkey after disasters.²⁸ There is no published data for the possible negative psychological outcome of cancer patients after an earthquake.

In breast cancer patients, stress, depression, and anxiety are frequently observed. The prevalence was 14.7%, 28.4%, and 43.2% respectively.²⁹ Also, depression in partners of patients increased among breast cancer patients.³⁰ In a Japanese study investigating the effect of the Fukushima earthquake on chronic diseases, cancer patients had an increased risk for psychological depression. Also, in another study, couples receiving cancer treatment had been negatively affected by the Fukushima earthquake. Women were more prone to psychological distress compared to men.^{31,32} In a study evaluating Hispanic cancer survivors and the normal population after Hurricane Maria in Puerto Rico, no difference was observed in terms of psychological health. Interestingly this study showed increased inflammatory markers in cancer survivors compared to the control group. The median time after the disaster was 7 months which may hide the psychological effects of disaster on survivors. Also, the cancer patients in this study were in remission and not receiving any treatment.³³ Results showed that depression, anxiety, and stress problems were observed by more than 50% of earthquake survivors. Although there was a significant difference in terms of the stage between the study and control group, end-stage diseases were the same across groups and were considered to have zero effect on psychological status. Also, the earthquake survivors were on lower chemotherapy doses compared to the resident group which may have positive effect on psychological status and would be unrelated with chemotherapy associated anxiety. Even though earthquake survivors received less chemotherapy than resident patients, they had worse psychological outcomes which may be attributed to the earthquakes. In accordance with other studies, women had worse depression and anxiety categories when compared to the control group. Nakaya et al. reported that there was an increased partner burden in chronic conditions resulting in psychological problems.³² This study showed increased stress, depression, and anxiety among cancer patients who are earthquake survivors. As the study hypothesized, earthquake-survivor cancer patients need more psychological support compared to regular cancer patients and may have worse outcomes compared to earthquake survivors without cancer. There may be need of more psychological and social support for cancer patients experienced earthquakes.

Conclusion

Recent earthquakes in Turkey had psychological negative effects on oncology patients. The increased stress, depression, and anxiety levels were observed in earthquake survivors who were evacuated from the disaster zone compared to the control group. More intensive studies are needed to investigate the long-term psychological effect of disasters on cancer patients.

Supplementary material. To view supplementary material for this article, please visit <https://doi.org/10.1017/dmp.2024.62>

Acknowledgments. Thank you to Miss Nurten Borazan for collecting data information.

Funding statement. The study did not receive any funding from non-commercial or commercial organizations.

Competing interests. The author does not declare any conflict of interest.

References

1. Man RX, Lack D, Wyatt C, *et al.* The effect of natural disasters on cancer care: a systematic review. *Prehosp Disaster Med.* 2019;34(s1):s48-s48. doi: [10.1017/S1049023X19001146](https://doi.org/10.1017/S1049023X19001146)
2. Ozaki A, Tsubokura M. Radiation oncology and related oncology fields in the face of the 2011 "triple disaster" in Fukushima, Japan. *Int J Radiat Oncol Biol Phys.* 2018;100(4):845-848. doi: [10.1016/J.IJROBP.2017.12.285](https://doi.org/10.1016/J.IJROBP.2017.12.285)
3. Ozaki A, Leppold C, Sawano T, *et al.* Social isolation, and cancer management - advanced rectal cancer with patient delay following the 2011 triple disaster in Fukushima, Japan: a case report. *J Med Case Rep.* 2017;11(1). doi: [10.1186/S13256-017-1306-3](https://doi.org/10.1186/S13256-017-1306-3)
4. Ozaki A, Tsubokura M, Leppold C, *et al.* The importance of family caregiving to achieving palliative care at home: a case report of end-of-life breast cancer in an area struck by the 2011 Fukushima nuclear crisis: a case report. *Medicine.* 2017;96(46). doi: [10.1097/MD.00000000000008721](https://doi.org/10.1097/MD.00000000000008721)
5. Ozaki A, Nomura S, Leppold C, *et al.* Breast cancer patient delay in Fukushima, Japan following the 2011 triple disaster: a long-term retrospective study. *BMC Cancer.* 2017;17(1). doi: [10.1186/S12885-017-3412-4](https://doi.org/10.1186/S12885-017-3412-4)
6. ReliefWeb. Türkiye: 2023 earthquakes situation report No. 8. Published March 9, 2023. Accessed July 3, 2023. <https://reliefweb.int/report/turkiye/turkiye-2023-earthquakes-situation-report-no-8-9-march-2023>
7. Anadolu Ajansı. Sağlık Bakanı Koca: 10 ilde 17 bin 929'u hekim olmak üzere 143 bin 829 personelimiz hizmet veriyor. Accessed July 3, 2023. <https://www.aa.com.tr/tr/asrin-felaketi/saglik-bakani-koca-10-ilde-17-bin-929u-hekim-olmak-uzere-143-bin-829-personelimiz-hizmet-veriyor/2813793#>
8. Ileri Haber. 'Depremde hastanelerin çoğu kullanılamaz hale geldi.' Accessed July 7, 2023. <https://www.ilerihaber.org/icerik/depremdede-hastanelerin-cogu-kullanilamaz-hale-geldi-151283>
9. Yilmaz V. A statistical analysis of the effects on survivors of the 1999 earthquake in Turkey. *Soc Behav Pers.* 2004;32(6):551-558. doi: [10.2224/SBP.2004.32.6.551](https://doi.org/10.2224/SBP.2004.32.6.551)
10. Sato D, Sato D. Evaluation of the long-term changes in fatigue of cancer survivors who received outpatient chemotherapy in the area affected by the Great East Japan Earthquake. *Open J Nurs.* 2021;11(7):566-577. doi: [10.4236/OJN.2021.117048](https://doi.org/10.4236/OJN.2021.117048)
11. Hopkinson J. Psychosocial support in Cancer Cachexia Syndrome: the evidence for supported self-management of eating problems during radiotherapy or chemotherapy treatment. *Asia Pac J Oncol Nurs.* 2018;5(4):358-368. doi: [10.4103/APJON.APJON_12_18](https://doi.org/10.4103/APJON.APJON_12_18)
12. Berger W, Coutinho ESF, Figueira I, *et al.* Rescuers at risk: a systematic review and meta-regression analysis of the worldwide current prevalence and correlates of PTSD in rescue workers. *Soc Psychiatry Psychiatr Epidemiol.* 2012;47(6):1001-1011. doi: [10.1007/S00127-011-0408-2](https://doi.org/10.1007/S00127-011-0408-2)
13. Johnson H, Thompson A. The development and maintenance of post-traumatic stress disorder (PTSD) in civilian adult survivors of war trauma and torture: a review. *Clin Psychol Rev.* 2008;28(1):36-47. doi: [10.1016/J.CPR.2007.01.017](https://doi.org/10.1016/J.CPR.2007.01.017)
14. Cardoso F, Kyriakides S, Ohno S, *et al.* Early breast cancer: ESMO clinical practice guidelines for diagnosis, treatment, and follow-up. *Ann Oncol.* 2019;30(8):1194-1220. doi: [10.1093/ANNONC/MDZ173](https://doi.org/10.1093/ANNONC/MDZ173)
15. Charalampopoulou M, Kritseli E, Chrousos GP, *et al.* Efficacy of stress management and psychosocial interventions on body image in breast cancer survivors - a systematic review. *Dialogues in Clin Neuro Mental Health.* 2019;2(4):237-242. doi: [10.26386/OBRELA.V2I4.136](https://doi.org/10.26386/OBRELA.V2I4.136)
16. Shim EJ, Lee JW, Cho J, *et al.* Association of depression and anxiety disorder with the risk of mortality in breast cancer: a National Health Insurance Service study in Korea. *Breast Cancer Res Treat.* 2020;179(2):491-498. doi: [10.1007/S10549-019-05479-3](https://doi.org/10.1007/S10549-019-05479-3)
17. Peng L, Huang W, Zhang W, *et al.* Psychometric properties of the short form of the fear of cancer recurrence inventory (FCRI) in Chinese breast cancer survivors. *Front Psych.* 2019;10:537. doi: [10.3389/FPSYT.2019.00537](https://doi.org/10.3389/FPSYT.2019.00537)
18. Tang Y, Fu F, Gao H, *et al.* Art therapy for anxiety, depression, and fatigue in females with breast cancer: a systematic review. *J Psychosoc Oncol.* 2019;37(1):79-95. doi: [10.1080/07347332.2018.1506855](https://doi.org/10.1080/07347332.2018.1506855)
19. LeVasseur N, Li H, Cheung W, *et al.* Effects of high anxiety scores on surgical and overall treatment plan in patients with breast cancer treated with Neoadjuvant therapy. *Oncologist.* 2019;25(3):212-217. doi: [10.1634/theoncologist.2019-0512](https://doi.org/10.1634/theoncologist.2019-0512)
20. Hashemi SM, Hormozi M, Allahyari A, *et al.* The prevalence of depression, anxiety, and stress in patients with breast cancer in Southeast Iran in 2019: a cross-sectional study. *Oncol Clin Pract.* 2020;16(3):104-108. doi: [10.5603/OCP.2020.0015](https://doi.org/10.5603/OCP.2020.0015)
21. DASS-21. The psychometric properties of the Turkish version of Depression Anxiety Stress Scale-21 (DASS-21) in health control and clinical samples. [Depresyon Anksiyete Stres-21 Ölçeğinin (DASÖ-21) Normal ve Klinik Örneklemde Türkçe Versiyonun Psikometrik Özellikleri]. Accessed April 7, 2023. https://www.researchgate.net/publication/322238323_The_Psychometric_Properties_of_Turkish_Version_of_Depression_Anxiety_Stress_Scale-21_DASS-21_in_Health_Control_and_Clinical_Samples_Depresyon_Anksiyete_Stres-21_Olceginin_DASO-21_Normal_ve_Klinik_Orne
22. Alacacioglu A, Tarhan O, Alacacioglu I, *et al.* Depression and anxiety in cancer patients and their relatives. www.jbuon.com. Accessed October 31, 2023.
23. Shi P-J. Theory and practice on disaster system research in a fifth time. *J Nat Disast.* 2009;18:1-9. https://www.researchgate.net/publication/285753303_Theory_and_practice_on_disaster_system_research_in_a_fifth_time. Accessed February 24, 2023.
24. Raeissi P, Sharifi M, Khosravizadeh O, *et al.* Survey of cancer patient safety culture: a comparison of chemotherapy and oncology departments of Teaching Hospitals of Tehran. *Asian Pac J Cancer Prev.* 2017;18(10):2775-2780. doi: [10.22034/APJCP.2017.18.10.2775](https://doi.org/10.22034/APJCP.2017.18.10.2775). Accessed February 24, 2023.
25. Kessler RC, Wang PS, Kendrick D, *et al.* Hurricane Katrina's impact on the care of survivors with chronic medical conditions. *J Gen Intern Med.* 2007;22(9):1225-1230. doi: [10.1007/S11606-007-0294-1](https://doi.org/10.1007/S11606-007-0294-1)
26. Heidari M, Ghodusi M. The relationship between body esteem and hope and mental health in breast cancer patients after mastectomy. *Indian J Palliat Care.* 2015;21(2):198-202. doi: [10.4103/0973-1075.156500](https://doi.org/10.4103/0973-1075.156500)
27. Tang B, Liu X, Liu Y, *et al.* A meta-analysis of risk factors for depression in adults and children after natural disasters. *BMC Public Health.* 2014;14(1):1-12. doi: [10.1186/1471-2458-14-623/FIGURES/2](https://doi.org/10.1186/1471-2458-14-623/FIGURES/2)
28. Ünsal O, Yazici O, Özdemir N, *et al.* Earthquake disaster impact on health care of cancer patients: single center experience. *Turkish J Internal Med.* 2023;5(4):234-239. doi: [10.46310/TJIM.1327111](https://doi.org/10.46310/TJIM.1327111)
29. Hashemi SM, Rafiemanesh H, Aghamohammadi T, *et al.* Prevalence of anxiety among breast cancer patients: a systematic review and meta-analysis. *Breast Cancer.* 2020;27(2):166-178. doi: [10.1007/S12282-019-01031-9](https://doi.org/10.1007/S12282-019-01031-9)
30. Nakaya N, Saito-Nakaya K, Bidstrup PE, *et al.* Increased risk of severe depression in male partners of women with breast cancer. *Cancer.* 2010;116(23):5527-5534. doi: [10.1002/CNCR.25534](https://doi.org/10.1002/CNCR.25534)
31. Nakaya N, Nakamura T, Tsuchiya N, *et al.* The association between medical treatment of physical diseases and psychological distress after the Great East Japan Earthquake: the Shichigahama Health Promotion Project. *Disaster Med Public Health Prep.* 2015;9(4):374-381. doi: [10.1017/DMP.2015.52](https://doi.org/10.1017/DMP.2015.52)
32. Nakaya N, Narita A, Tsuchiya N, *et al.* Partners' ongoing treatment for chronic disease and the risk of psychological distress after the Great East Japan Earthquake. *Tohoku J Exp Med.* 2016;239(4):307-314. doi: [10.1620/TJEM.239.307](https://doi.org/10.1620/TJEM.239.307)
33. Rodriguez-Rabassa M, Hernandez R, Rodriguez Z, *et al.* Impact of a natural disaster on access to care and biopsychosocial outcomes among Hispanic/ Latino cancer survivors. *Sci Reports.* 2020;10(1):1-12. doi: [10.1038/s41598-020-66628-z](https://doi.org/10.1038/s41598-020-66628-z)