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COVID and cancer

COVID-19 Impact on Newly Diagnosed Breast Cancers at Regional Cancer Centre, Thiruvananthapuram—An Audit

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Abstract

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The coronavirus pandemic has created havoc in every aspect of life including cancer care and was declared a pandemic. This audit was conducted to study the impact of the pandemic on diagnosis and treatment of newly diagnosed breast cancer patients at a tertiary cancer center in South India. A total of 1,647 patients who registered at Regional Cancer Centre (RCC), Thiruvananthapuram, Kerala, India for breast cancer during the period April 1, 2020, to September 30, 2020 (COVID-19 period) as well as April 1, 2019, to September 30, 2019 (pre-COVID-19 period) were included in the study. Data regarding the geographic distribution, stage at presentation, time factors for reporting for care, diagnosis, and treatment, referral for care elsewhere were collected and analyzed. The study was approved by the Institutional Review Board. Means and ranges were calculated for continuous type variables, and numbers and percentages for categorical variables. To determine whether there were significant differences between the two groups, independent *t*-test was used for continuous variables and chi-square test for categorical type of variables. A notable reduction (36%) in newly diagnosed breast cancer patients was seen in 2020 when compared with 2019. There was a significant difference in the geographic distribution of patients in both cohorts ($p = 0.001$) and a notable reduction in the number of patients reporting to RCC for treatment from the northern districts of Kerala (81%) and outside Kerala (89.5%). There was no significant difference in the time (in weeks) since symptom onset and reporting to hospital or the clinical stage at diagnosis between the groups. Also, coronavirus disease 2019 (COVID-19) did not seem to negatively impact time

Keywords
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- newly diagnosed
- impact
- audit

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intervals between date of registration and pathological diagnosis or start of primary treatment. More patients received neoadjuvant systemic therapy during 2020 compared with 2019, and this difference was statistically significant ($p = 0.004$). There was no difference in the type of surgery (breast-conserving surgery vs. modified radical mastectomy). The results demonstrate that COVID-19 did not appear to negatively impact the diagnosis and treatment of newly diagnosed breast cancer patients. However, this is largely attributable to the significantly less number of patients who registered, for whom the departments were able to maintain timely cancer care despite the difficult pandemic times. Significantly more patients received neoadjuvant systemic therapy in 2020.

Introduction

Breast cancer is the most commonly diagnosed tumor with 2.3 million cases in 2020 representing 11.7% of all cancer cases and the fifth leading cause of cancer mortality with 685,000 deaths worldwide.[1] In India, breast cancer accounted for 13.5% (178,361) of all cancer cases and 10.6% (90,408) of all deaths as per the GLOBOCAN data 2020.[2] The coronavirus disease 2019 (COVID-19) pandemic had spread all over the world creating havoc in every aspect of life from health care to the economy and was declared a pandemic in March 2020.[3] Consequently, there was a complete reorganization of the health system, including reallocation of crucial human and economic health resources toward care of COVID-19 patients. Also, people were frightened; older patients and those with existing health conditions were forced to isolate themselves as much as possible. This reduced the number of people seeking health care. All these had a strong impact on new cancer diagnoses.[4] Ferrara et al from Italy showed a 38.2% decrease in new breast cancer diagnoses.[5] A multicenter analysis of early breast cancer patients from Hubei, China reported that breast cancer diagnosis rates were 5.2% in Hubei where strict lockdown measures were in place but were 15.3% in provinces where lockdown measures were not in place.[6] Data from 41 cancer centers across India demonstrate that cancer care was widely affected by the COVID-19 pandemic. There was a substantial decline in the number of new registrations, follow-up visits, cancer surgeries, radiotherapy and chemotherapy sessions.[7] The delay in diagnosis and treatment interruptions is likely to cause a stage migration and higher cancer-related mortality in the coming years. The aim of this audit is to study the impact of the COVID-19 pandemic on diagnosis and treatment of newly diagnosed breast cancer patients at a tertiary cancer center in south India.

Material and Methods

This study analyzed the data of all the patients who were registered at the Regional Cancer Centre (RCC), Thiruvananthapuram, Kerala, India for breast cancer during the period April 2020, to September 2020 (COVID-19 period) as well as April 2019, to September 2019 (pre-COVID-19 period). A total of 1,005 patients had registered between April 2019, and September 2019, and 642 patients during the period April 2020, to September 2020, with newly diagnosed breast cancer. The study was approved by the Institutional Review Board. Patients' records were reviewed and data on patient demographics, clinical, treatment, and follow-up details were captured in a structured datasheet.

The following factors were assessed:

1. Geographic distribution (district-wise).
2. Time since symptom onset and reporting to a local hospital and RCC.
3. Clinical stage at presentation.
4. Average time since date of registration to date of pathological confirmation at RCC.
5. Average time since date of registration to date of commencement of treatment (surgery or systemic therapy).
6. Average time to date of start of radiotherapy after completion of chemotherapy or following surgery (for those who are postneoadjuvant systemic therapy).
7. Number of patients who were referred elsewhere for commencing or continuation of treatment.

Statistical Analysis

Means and ranges were calculated for continuous type variables, and numbers and percentages for categorical variables. To determine whether there were significant differences between the two groups, independent *t*-test was used for continuous variables and chi-square test for categorical type of variables.

Results

A total of 1,647 patients were included in the study. There was a 36% reduction in newly diagnosed breast cancer patients in 2020 when compared with 2019 (642 vs. 1,005). The mean age of the patients registered in 2019 was 53.5 years (22–92 years) and in 2020 was 54 years (26–91 years) ($p = 0.22$). There was no significant difference in histological or molecular subtype between the groups, ductal histology, and luminal B subtype accounting for majority in both cohorts.

There was a significant difference in the geographic distribution of patients in both cohorts ($p = 0.001$). Thiruvananthapuram district is located in the southernmost end of Kerala. Of the 14 districts, Thiruvananthapuram, Kollam, Pathanamthitta, Kottayam, Alleppey, Idukki, and Ernakulam were considered as the southern districts and rest as northern districts. There was an 81% reduction in the number of

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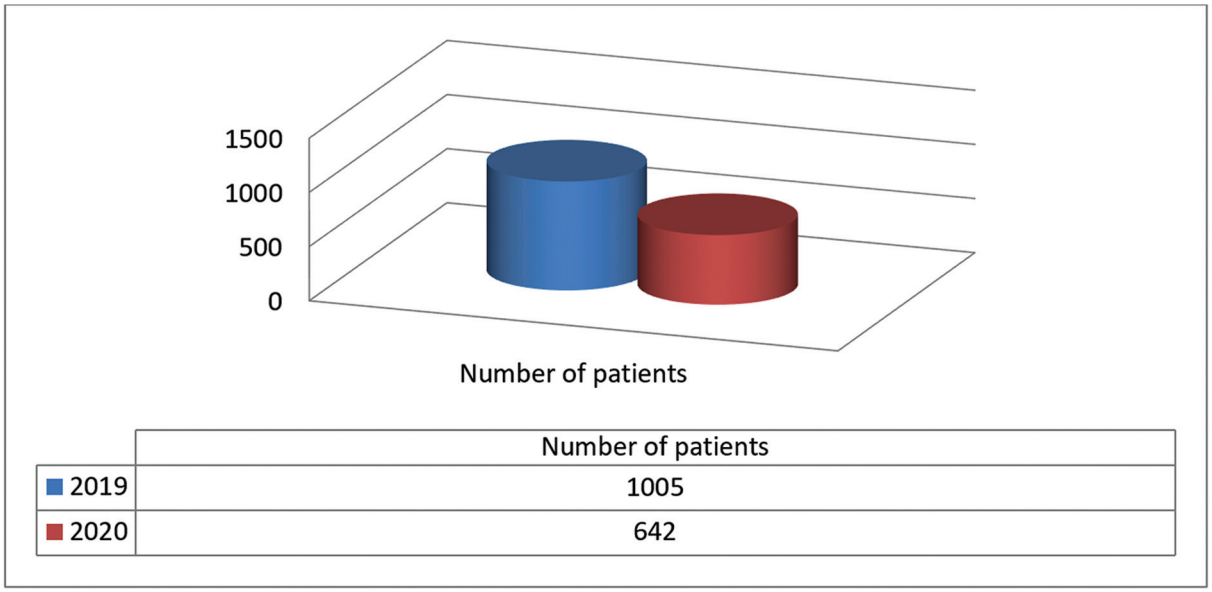

Fig. 1 Number of newly registered breast cancer patients in both cohorts.

patients reporting to RCC for treatment from the northern districts of Kerala (162 vs. 30) during the COVID-19 period. Likewise, there was an 89.5% reduction in number of patients reporting from outside the state of Kerala in the COVID-19 period (124 vs. 13). In 2020, of the 642 newly registered patients, 428 patients (66.6%) hailed from Thiruvananthapuram and Kollam districts.

There was no significant difference in the time (in weeks) since symptom onset and reporting to a local hospital and RCC in either cohort (23.2 vs. 22.8 weeks). A subgroup analysis of patients from Thiruvananthapuram and Kollam districts showed no significant difference in the time (in weeks) since symptom onset and reporting to a local hospital and RCC in either cohort (20.5 vs. 22.3 weeks). The most common stage at presentation was stage II in both cohorts (47.6 vs. 46.4%) followed by stage III (22.2 vs. 23.3%). No significant difference in clinical stage at diagnosis was noted between the two groups (►**Figs. 1**–**3**).

The average time since date of registration to date of pathological confirmation was 1.8 weeks in both cohorts ($p = 0.99$). The average time since date of registration to date of commencement of primary treatment, which was either

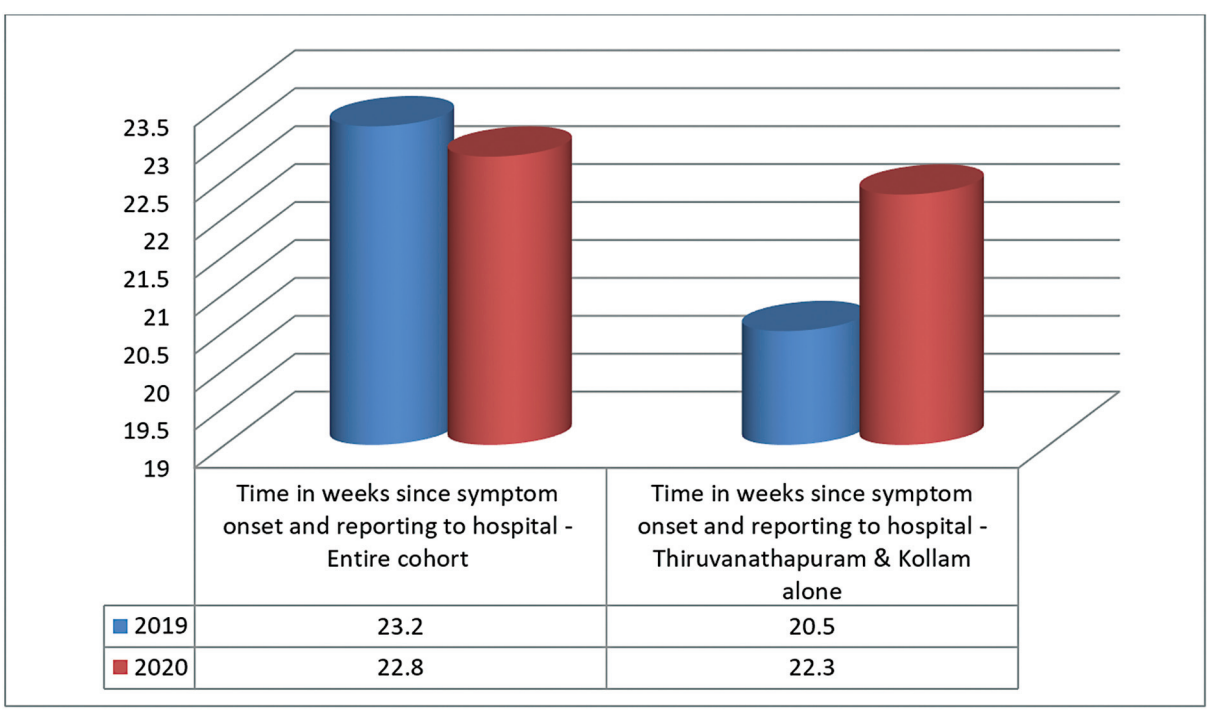

Fig. 2 Time intervals (weeks) since symptom onset and reporting to hospital or Regional Cancer Centre.

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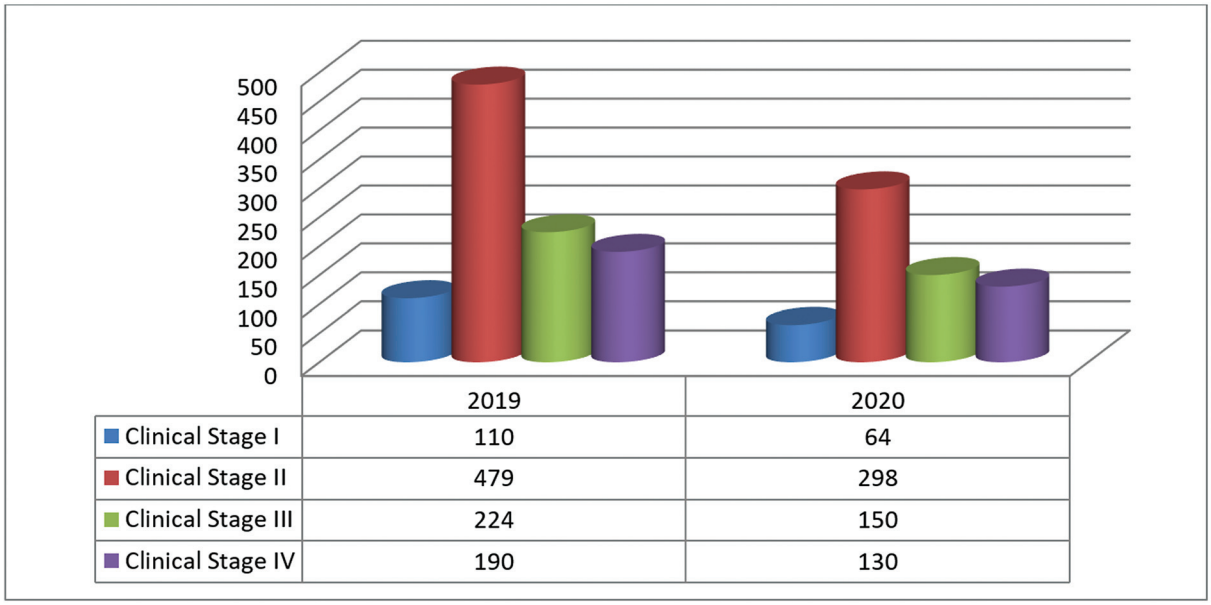

Fig. 3 The clinical stage-wise distribution in both groups.

surgery or systemic therapy depending on the clinical stage and/or molecular subtype, was 5.8 weeks in 2019 and 5.3 weeks in 2020 ($p = 0.39$). The average time since date of registration to date of surgery was 5.9 weeks in 2019 and 6 weeks in 2020 ($p = 0.85$), and time since registration and start of neoadjuvant systemic therapy was 5.5 weeks in 2019 and 4.6 weeks in 2020 ($p = 0.30$). The average time interval to the start of radiotherapy after completion of adjuvant chemotherapy or following surgery (for those who were postneoadjuvant systemic therapy) was 2.6 weeks longer in 2020, but this was not statistically significant (9.5 vs. 12.1) ($p = 0.35$). Fewer patients were referred elsewhere for commencing or continuation of treatment in 2020 compared with 2019. Only 98 patients (15%) were referred outside RCC for treatment in 2020 compared with 267 patients (27%) in 2019, and this difference was statistically significant ($p < 0.001$) (►**Fig. 4**).

Nearly 85% of patients underwent curative intent therapy in both years. Six hundred and three (60%) patients underwent primary surgery in 2019 compared with 335 patients (52.2%) in 2020. More patients received neoadjuvant systemic therapy in 2020 compared with 2019 (31.9 vs. 25%; $p = 0.004$). Among

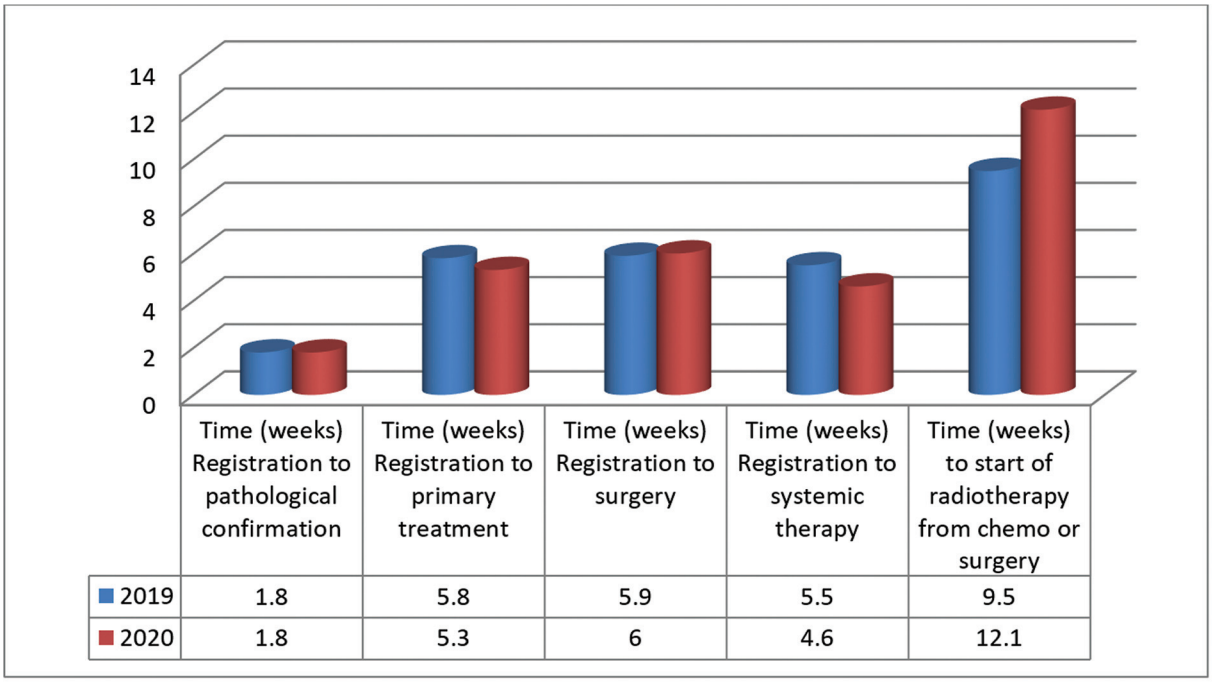

Fig. 4 Time intervals (weeks) to registration and diagnosis and treatment in both groups.

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patients who received neoadjuvant systemic therapy, most received neoadjuvant chemotherapy, only five patients received neoadjuvant endocrine therapy (one patient in 2019 and four patients in 2020). The type of surgery did not differ between the two cohorts; the proportion of patients who underwent breast-conserving surgery (BCS) were 30.9 and 31.8% and modified radical mastectomy (MRM) were 69.1 and 68.2% in 2019 and 2020, respectively ($p = 0.74$). All patients in either cohort who required adjuvant radiation received hypofractionated radiotherapy dose of 40 Gy in 15 fractions, 5 fractions a week for 3 weeks with a boost of 10 Gy in 5 fractions for those with a conserved breast.

Discussion

The COVID-19 pandemic created havoc in every aspect of life from health care to the economy and was declared a pandemic in March 2020.[3] Consequently, there was a reorganization of the health system, including reallocation of crucial human and economic health resources toward the care of COVID-19 patients. This adversely affected the delivery of cancer services throughout the world.[8] This institute continued to provide cancer services—albeit scaled down—even during lockdown period. Outpatient visits were restricted to those with new diagnosis of cancer or relapse and those on active cancer-directed treatment. Surgeries were stopped during the initial days of total lockdown. Systemic therapies and radiotherapy which were already commenced were continued as scheduled with safety measures. Patients with high-risk disease such as human epidermal growth factor receptor-2-positive and triple-negative cancers were prioritized for commencing therapy. Nevertheless, due to the logistic constraints posed by the lockdown, many patients were unable to access the cancer care services. A decline in cancer diagnoses was observed in most countries and for almost all tumor sites.[4,9] This analysis shows a steep reduction (36%) in new patients with breast cancer in 2020 at RCC compared with the prepandemic period which is similar to findings reported in Italy.[5,10] There was no significant difference in the time (in weeks) since symptom onset and reporting to hospital, and also the clinical stage at diagnosis was not different between the two cohorts. The most common stage at presentation was stage II in both cohorts (47.6 vs. 46.4%) followed by stage III (22.2 vs. 23.3%). This is in contrast to few studies that reported stage migration to advanced stages at presentation of patients with breast cancer.[10–12] There was a significant difference in the geographic distribution of patients, with fewer patients reporting to this institute which is located in southernmost end of Kerala from northern districts of Kerala in 2020 compared with 2019. Only 13 patients reported from outside Kerala in 2020 compared with 124 patients in 2019. This was due to the strict lockdown and travel restrictions initiated by the government during the COVID-19 times.[13]

This analysis did not show any statistically significant difference in terms of time to diagnosis, initiation of systemic therapy, surgical and radiation therapy procedures between the two cohorts. The average time since date of registration to date of pathological confirmation and commencement of treatment was similar in 2020 and 2019. These results demonstrate that COVID-19 did not appear to negatively impact the diagnosis and treatment of newly diagnosed breast cancer patients at our center. It is recognized that the significant decline in the total number of patients registered is the reason for this. Few studies from Italy have also reported similar results with no reported delay in diagnosis and treatment.[10,14] A delay in treatment has been reported in India[15] and many countries due to reallocation of health resources toward care of COVID-19 patients.[6,16] There is growing concern that these delays would have an impact on oncological outcomes in the years to come. The National Cancer Institute has predicted as many as 10,000 additional deaths during the next 10 years due to the delayed diagnosis of breast and colorectal cancers in the United States as a result of the pandemic.[17] Since there was no significant delay in diagnosis and treatment for the patients in this study, we expect similar outcomes as compared with the prepandemic period. Fewer patients were referred elsewhere from our institution for commencing or continuation of treatment in 2020 compared with 2019. This could be because of the decrease in total number of breast cancer patients registered in 2020, and these patients were mostly hailing from southern districts of Kerala and hence did not need to be referred elsewhere.

There was no significant difference in the intent of treatment in either cohort. However, significantly, more patients received neoadjuvant systemic therapy as surgical procedures were delayed during the COVID-19 period. This has been reported in other studies as well.[18] The number of patients undergoing BCS and mastectomy were similar in both cohorts which is similar to that reported in other studies.[19,20] All patients who received adjuvant radiation were treated on hypofractionated 3-week schedule which has been the standard practice at this institution for several years.

The limitations of the study are its retrospective nature and the inherent bias associated with such a design. Another disadvantage is that clinical outcomes of patients were not analyzed. The effect on patients who were unable to seek timely diagnosis and treatment during the COVID-19 lockdown could not be assessed by this study. Such patients may likely be the cause of significant decrease in breast cancer survival in the ensuing years. Being a single institutional analysis, the results can be influenced by this institution's practice patterns which could be different from other centers during the pandemic.

Conclusion

This study did not show a negative impact from COVID-19 in terms of time to diagnosis and treatment of newly diagnosed breast cancer reporting to this institution. It is recognized that the significant decline in the total number of patients registered is the reason for this. More patients received neoadjuvant systemic therapy as opposed to primary surgery.

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Authors' Contribution

G.B. performed the literature search, collected the data, and prepared the manuscript. K.K.R. was involved in the design of the study and preparation of the manuscript. A.M. was involved in the statistical analysis and preparation of manuscript. B.P., A.A., P.A., K.C., R.J., and N.R. were involved in the design of the study. R.B. was involved in the design of the study and preparation of manuscript. B.S.M. designed the study, supervised the conduct of the study, interpreted results, and edited the manuscript.

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None.

Conflict of Interest

None declared.

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