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Short Communication

The impact of COVID-19 on cardio-oncology care in Taiwan



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COVID-19 has not only affected the respiratory but the cardiovascular system. Taiwan has encountered a less severe COVID-19 pandemic. We reported the current situation in Taiwan. In this study, we retrospectively analyzed the data from our cardio-oncology program since October of 2019 to April of 2020 (the initial months of COVID-19 pandemic). In our cardio-oncology program, newly diagnosed breast cancer patients preparing for epirubicin therapy were included. Echocardiography, 6-min walking distance and major adverse cardiovascular events (MACEs) were recorded. To evaluate whether the social atmosphere affects cardio-oncology care, we analyzed the objective (physical) and subjective (emotional) parameters before and after January 21, 2020, when the first case of COVID-19 was confirmed in Taiwan. There was no significant decrease in patients' return ratio and LVEFs. However, there was a trend of subjective shortness of breath reported by the patients but no decline in 6 MWT. Notably, none of the enrolled patients reported MACEs during the COVID pandemic. We observed an impact of anxiety on patients receiving epirubicin but it did not influence their return ratio.

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Introduction

SARS-CoV-2 causing COVID-19 has reached a pandemic level, which not only affects the respiratory system but also the cardiovascular system.¹ The majority of infected populations who die have underlying comorbidities. Also, patients infected by SARS-CoV-2 with a cardiovascular or malignant disease have an elevated risk of adverse outcomes.² Most importantly, the impact of COVID-19 on the health care system has reached a non-negligible level.^{3,4} It is clear that the effect of COVID-19 goes beyond the disease per se but also compromises daily medical supplies. To note, cancer patients seem to be more susceptible to SARS-CoV-2 and have more severe symptoms. However, in areas with high SARS-CoV-2 transmission rates, to avoid frequent hospital visits and anticancer therapy or elective surgery may be individually considered for patients with stable cancer.⁵ In these cases, oncologists need to balance the risks and benefits.

As one of the first countries to activate public health measures, Taiwan has encountered a less severe COVID-19 pandemic than many other countries. On July 17, 2020, there were 452 confirmed cases with 7 deaths in Taiwan, compared with 13,547,206 cases with 584,058 deaths globally.⁶ Instead of lockdown, currently most health care facilities in Taiwan are maintaining their medical services, including cardio-oncology care. Despite the minor physical impact of COVID-19, the unprecedented level of real-time information also leads to an air of anxiety in Taiwan. The daily deluge of infection numbers also adds a frightening dimension to our understanding of the virus's worldwide spread.

Herein, we investigated the impact of COVID-19 on cardio-pulmonary performances in patients with breast cancer in Taiwan. Through monitoring the adherence, changes of left ventricular ejection fraction (LVEF), subjective dyspnea and 6-min walking test (6 MWT), we studied the objective (physical) and subjective (emotional) parameters before and after January 21st on which the first case was diagnosed of COVID-19 in Taiwan.

Methods

In this study, we retrospectively analyzed the data from our cardio-oncology program since October of 2019 to April of 2020 (the initial months of COVID-19 pandemic). At Chi-Mei Medical Center, Taiwan, we established a cardio-oncology program and enrolled newly diagnosed breast cancer patients preparing for epirubicin therapy since 2014. Echocardiography, 6 MWT and adverse cardiovascular events including new onset of hypertension, HF, ischemic stroke, enzyme-positive myocardial infarction (MI), and all-cause mortality were recorded at baseline, three months (during chemotherapy) and six months (post chemotherapy). In addition, dyspnea assessment (modified Borg scale) was measured from 0 (none) to 10 (severe shortness of breath)

Table 1 The baseline characteristics of the breast cancer patients (N = 203) under Cardio-Oncology Program.

| | Cardio-Oncology Program (n = 203) |
|--|-----------------------------------|
| Demographic parameters | |
| Age (years) | 54.2 ± 10.8 |
| height (cm) | 157.2 ± 12.4 |
| Body weight (kg) | 59.8 ± 14.8 |
| Heart rate (bpm) | 82.4 ± 12.3 |
| Systolic blood pressure (mmHg) | 120 ± 18.4 |
| Diastolic blood pressure (mmHg) | 75 ± 8.3 |
| Respiratory rate (rpm) | 12 ± 4.6 |
| DM, n (%) | 5 (2.4) |
| HTN, n (%) | 18 (8.8) |
| Hyperlipidemia, n (%) | 18 (8.8) |
| CKD, n (%) | 2 (0.9) |
| Laboratory parameters | |
| Creatinine clearance rate (ml/min) | 87.6 ± 30.5 |
| Serum glucose (ac, mg/dl) | 90.2 ± 10.5 |
| Triglyceride (mg/dl) | 139.2 ± 10.2 |
| Cholesterol (mg/dl) | 178.6 ± 35.4 |
| NT-proBNP (pg/ml) | 15.6 ± 10.8 |
| hsTnl (pg/ml) | 2.4 ± 1.9 |
| Anti-cancer therapies | |
| Cancer stage | |
| 1 | 46 (22.6) |
| 2 | 102 (50.2) |
| 3 | 35 (17.2) |
| 4 | 20 (9.8) |
| Operations, n (%) | 142 (69.9) |
| Mean single dose of epirubicin (mg/M ²) | 120.8 ± 15.4 |
| Accumulating dose of epirubicin (mg/M ²) | 308.7 ± 110.2 |
| Trastuzumab use, n (%) | 50 (24.6) |
| Concomitant radiotherapy, n (%) | 55 (27.1) |
| CV medications | |
| Anti-platelet/anti-coagulants, n (%) | 2 (0.9) |
| ACEIs/ARB, n (%) | 13 (6.4) |
| MRA, n (%) | 2 (0.9) |
| β-blockers, n (%) | 8 (3.9) |
| Statins, n (%) | 10 (4.9) |
| LVEF (%) | |
| Baseline | 76.6 ± 7.6 |
| During chemotherapy (3 months) | 74.5 ± 5.5 |
| After chemotherapy (6 months) | 72.5 ± 6.3 |
| 6MWT (m) | |
| Baseline | 374.6 ± 74.6 |
| During chemotherapy (3 months) | 395.1 ± 74.1 |
| After chemotherapy (6 months) | 396.8 ± 83.6 |

Table 1 (continued)

| | Cardio-Oncology Program (n = 203) |
|-------------------------------------|-----------------------------------|
| Dyspnea score (Modified Borg Scale) | |
| Baseline | 0 (0,0) |
| During chemotherapy (3 months) | 2 (0, 5) |
| After chemotherapy (6 months) | 1 (0, 3) |

Data are expressed as mean \pm SD, or median.

CKD = chronic kidney disease, CKD = chronic kidney disease; hsTnl = high-sensitivity troponin I; BNP = brain natriuretic peptide; ACEIs/ARB = Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blocker; MRA = mineralocorticoid receptor antagonist; LVEF = left ventricular ejection fraction; 6 MWT = 6-min walk test.

Breast cancer staged is based on AJCC staging systems.

according to the patients' statement at rest.⁷ A quality of life questionnaire, the EuroQol-5D (EQ (5D)) index, was administered before, during, and after anticancer therapies. In this cardio-oncology program, any functional decline was reported to oncologists to consider adjusting the regimens. Otherwise, cardiologists were consulted for cardiovascular risk education and management. The study was conducted in strict accordance with the Declaration of Helsinki and was approved by the local ethics committee (institutional review board approval no. 10411–008). The result represented in this work is not overlapped with any previous analyses.

Continuous data were presented as means \pm standard deviations while dichotomous data were presented as percentages. Chi-square tests or Fisher's exact tests were applied for categorical variables. Student's t-tests was applied for comparison upon the distribution of continuous variables. SPSS software (version 22.0, IBM SPSS Inc., Chicago, IL, USA) was used for statistical analyses.

Results

Among the 203 enrolled patients, the average ages were 54.2 ± 10.8 years-old while only a small amount of them

had comorbidities including hypertension, diabetes, hyperlipidemia and chronic kidney disease (Table 1). Most of the patients were at cancer stage 2. All of the patients received epirubicin while one quarter of them were also under Trastuzumab or radiotherapies. In Fig. 1A, there was no significant decrease in patients' return ratio (generally above 90%) at each visit. The echocardiography measured LVEFs were similar (approximately 70–78%). However, there was a trend of subjective shortness of breath (generally from one to five) reported by the patients enrolled at the dyspnea assessment but no decline in 6 MWT (Fig. 1B). In the quality of life analysis, the EQ5D index declined slightly in late January and February but recovered thereafter. This demonstrated that the global COVID-19 pandemic may influence, to a certain degree, the subjective symptoms of patients undergoing anticancer therapies. Notably, there was no delay or postponing of therapies. After all the included patients completed the monitoring at baseline, post three months and six months, the LVEF slightly dropped while no significant changes regarding 6 MWT and dyspnea index (Table 1).

Discussion

Despite an impact of anxiety on patients receiving epirubicin therapies, our findings indicated that the pandemic of COVID-19 did not influence their adherence and myocardial function. Although there were subjective complaints of dyspnea in patients receiving epirubicin therapy, LVEF and 6 MWT showed no specific decline. Different from many other countries, patients in Taiwan have the privilege of access to the regular medical services, including cardio-oncology care. Patients with cancer seem to be more likely to be diagnosed with COVID-19. Among 1524 patients admitted to the Department of Radiation and Medical Oncology in Zhongnan Hospital at Wuhan University, compared with the incidence of COVID-19 diagnosis in 0.37% in the general population, cancer patients had a higher incidence of 0.79%.⁸ Although the majority of adult patients infected with SARS-CoV2 present with symptoms, cancer

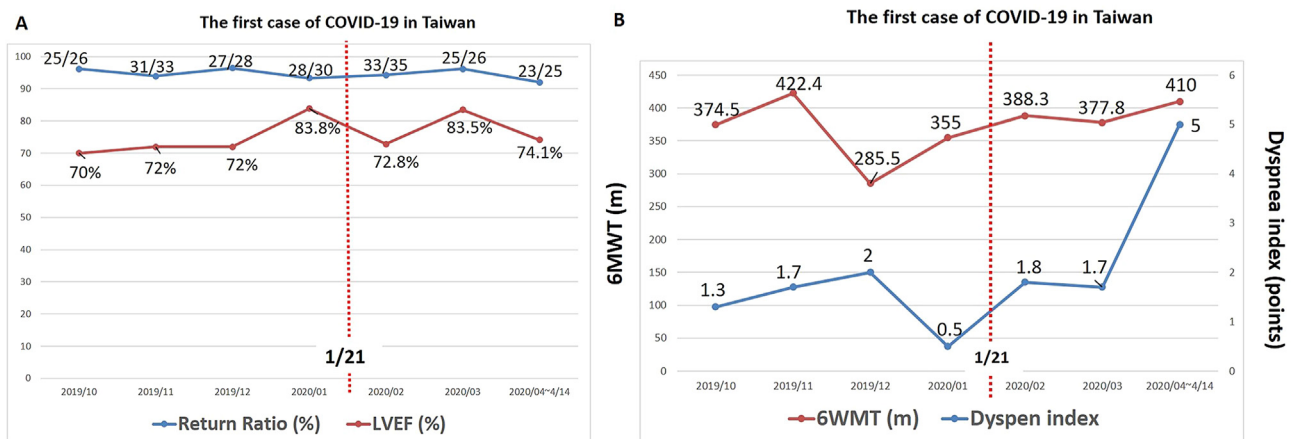


Figure 1 (A) The return ratio (blue line; represented as number of patients) and left ventricular ejection fraction (LVEF; red line) before and after January 21st, 2020 when the first case of COVID-19 was confirmed in Taiwan (B) A trend of increasing severity of shortness of breath (blue line; from 1.3 to 5) but no decline in 6 min walking test (6 MWT; red line; average from 374.5 m to 410 m) before and after January 21st, 2020 when the first case of COVID-19 was confirmed in Taiwan.

patients may not have typical symptoms due to their declined immune systems, especially post treatment of anticancer therapies. Although patients with cancer are more vulnerable to COVID-19, at present there is no guidance for these patients to defer cancer treatment. However, in areas with high SARS-CoV-2 transmission rates, to avoid frequent hospital visits and anticancer-related immune compromise, postponing anticancer therapy or elective surgery may be individually considered for patients with stable cancer.⁹ In these cases, oncologists need to balance the risks and benefits.

Given that the pandemic has not yet plateaued, we should remain prepared for future challenges to maintain our medical service. We have rapidly expanded telemedicine hardware and software in case patients or caregivers are mandated for quarantine. Any non-urgent procedures are recommended to be deferred. By sharing our experiences, we expect to establish a platform to communicate with other cardio-oncology teams and hopefully discover an optimal strategy for treating particularly vulnerable patients.

Conclusions

Collectively, although cardio-oncology programs are currently emerging worldwide, there are few reports delineating their actual efficacy and benefit, especially during a pandemic. We observed an impact of anxiety on patients but it did not influence their return ratio for monitoring of cardiotoxicity.

Author contributions

All authors were involved in the conception and design of the study and data interpretation. WC and YF drafted the paper and performed data analysis. WC and YF were involved in the data analysis and interpretation. All authors critically revised the paper and approved it for submission.

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Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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