Targeted therapies, which include monoclonal antibodies and kinase inhibitors (KIs), have been introduced to treat cancer for 20 years. Anti-HER2 therapies (trastuzumab, pertuzumab) and tyrosine kinase inhibitors (lapatinib, olaparib) have revolutionized breast cancer treatment in terms of improving survival.2,3 Despite their critical role in cancer treatment, these therapies were also reported with many cardiac adverse events. Incidence rate of congestive heart failure for trastuzumab in a real-world study is 2.8%, which is higher than report from clinical trials.3 A meta-analysis showed that trastuzumab increased risk of high-grade congestive heart failure in comparison with placebo.4 Cardiotoxicity is also observed with other targeted therapies such as pertuzumab and lapatinib, although not as commonly as with trastuzumab.5,6 Cardiotoxicity may exist in restricted indication of drug and impact patient’s life quality. However, the use of targeted therapy is irreplaceable in breast cancer patients, particularly for patients with HER2-positive. A comprehensive understanding of factors affecting cardiotoxicity of targeted therapy is essential. In this study, we aimed to explore the influencing factors leading to targeted therapy-related cardiotoxicity and to provide recommendations for clinical practice based on the findings.

Methods

Data were collected from Taipei Medical University clinical research database (TMUCRD) which contains electronic medical records of 3 affiliated hospitals. All the datasets were mapped to the Observational Medical Outcome Partnership common data model. The database consists of pathology report, hospitalization details, patient self-payment items, drug prescription and some laboratory data. Between 2008 and 2020, breast cancer patients treated at TMU’s three affiliated hospitals were identified. We excluded patients aged younger than 20 years old and not treated with any of the studied targeted therapy (trastuzumab, pertuzumab, lapatinib, ribociclib, palbociclib, olaparib and everolimus). We also excluded patients who have preexisting cardiac diseases. The primary endpoint is cardiac adverse events, which consist of ischemia/myocardial infarction, QT prolongation/arrhythmia, conduction disorders, heart failure and coronary artery diseases. Covariates include demographic characteristics, cancer stage, tumor size, comorbidities and comedicaions. We applied logistic regression model to assess the association of each influencing factor with the outcome.

Results

A total of 288 patients were included in this study. For demographic characteristics, both univariate and multivariate analysis were showed that smoking and drinking were associated with cardiotoxicity. Other risk factors, such as hypertension, hyperlipidemia, diabetes, renal disease, and cerebrovascular disease, were also verified. Patients who use chemotherapy, as consistent with previous studies,7 had a higher risk of cardiotoxicity (OR = 2.95, 95% CI: 1.09-7.96, p-value = 0.033). Cardioprotective medications [statins, beta blockers, calcium channel blockers, angiotensin II receptor blockers] were associated with a decreased risk of CAEs while the use of aspirin increased the risk many times (OR = 15.61, 95% CI: 5.88-41.48, p-value < 0.001).

Conclusions

Results from our study showed that besides the well-known cardiac risk factors, the use of aspirin may significantly increase risk of cardiotoxicity in breast cancer patients treated with targeted therapy. Along with heart function assessment, cardioprotective drugs during oncology treatment should be considered for this population, particularly those who increased cardiovascular risk.

References