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Letters

RESEARCH LETTER

The United Kingdom's First Cardio-Oncology Service

A Decade of Growth and Evolution

The long-term outlook for oncology patients has significantly improved with the introduction of novel cancer therapies. However, this progress comes with the trade-off of increased cardiotoxicity rates, giving rise to a population of patients at higher risk for cardiovascular (CV) diseases. Notably, CV complications have become a leading cause of both treatment interruptions and mortality among cancer survivors.[1,2] Recognizing the necessity for specialized care, cardio-oncology services and collaborative clinical guidelines have been established worldwide.[3] In response to the fast-paced advancements in oncology, cardio-oncology has also undergone a rapid evolution to effectively meet the needs of this growing population.[4]

In this study, we describe how the first cardio-oncology service in the United Kingdom has evolved over a 10-year period. This evolution is a direct response to the changing shifts in the oncologic landscape, expanding from its initial focus as a heart failure subspecialty to a diverse medical specialty encompassing various domains of cardiology.

We prospectively recorded information from the initial encounter with patients referred to our service, spanning from February 2011 to December 2021. Subsequently, data collected from 1,499 patients were analyzed using Rstudio V1.4.1717 (RStudio). Patients were categorized based on the referral reason and compared. Note that this study was exempt from institutional ethics review because of its observational nature, which involved data collected for routine clinical purposes.

The mean age was 60 ± 15 years, with 60% of the population being female. The predominant tumor locations were in the breast (n = 427, 28.5%), hematologic sites (n = 151, 10.1%), and the gastrointestinal tract (n = 114, 7.6%). The average number of new referrals per month was 4.5 patients in 2011 and increased to 23 patients in 2021. Concurrently, the total number of outpatient consultations, accounting for both new referrals and follow-ups, increased from 61 in 2011 to 1,988 in 2021.

Among patients, one-third (32.8%) were referred for cancer therapy-related cardiac dysfunction (CTRCD), and 22.3% were referred for non-heart failure cardiovascular disease (non-HF CVD), including conditions such as arrhythmia, chest pain, hypertension, pericardial disease, and myocarditis. The remaining patients sought referrals for pretreatment assessment (39.0%), intracardiac masses (3.0%), survivor screening (1.9%), and direct complications of cancer (0.9%).

From 2012 to 2017, there was a notable predominance of CTRCD over non-HF CVD. This ratio underwent a shift from 2018 onward, with non-HF CVD emerging as a more frequent referral indication (**Figure 1A**), and patients on non-anthracycline-based therapies becoming increasingly referred (**Figure 1B**). Patients with CTRCD differed from those with non-HF CVD in several aspects; they were predominantly women (% male CTRCD: 28.2% vs non-HF CVD: 37.3%; $P = 0.029$), had a lower incidence of diabetes (CTRCD: 1.8% vs non-HF CVD: 7.2%; $P < 0.001$), and exhibited a lower prevalence of pre-existing CVD (CTRCD: 9.8% vs non-HF CVD: 16.7%; $P = 0.010$). Breast cancer was more prevalent in the CTRCD cohort (36.3% vs 24.5%; $P < 0.001$), whereas melanoma and lung cancer were more common among patients with non-HF CVD (5% vs 2.7%; $P = 0.049$ and 5% vs 1.8%; $P = 0.007$). Consequently, cancer treatment also varied between the 2 groups.

Anthracyclines and human epidermal growth factor receptor 2 (HER2)-targeted therapies were more prevalent in the CTRCD group (50% vs 29% and 32% vs 12%), whereas tyrosine kinase inhibitors (TKIs) and immune checkpoint inhibitors (ICIs) were dominant in the non-HF CVD cohort (9% vs 2% and 20% vs 4.2%). In the analysis of patients with CTRCD and non-HF CVD, a multivariable logistic regression model incorporating factors such as age, sex, history of hypertension, diabetes, pre-existing heart disease, dyslipidemia, obesity, smoking history, and oncologic drug groups (anthracyclines, TKIs, ICIs, fluoropyrimidines, proteosome inhibitors, and rapidly accelerated

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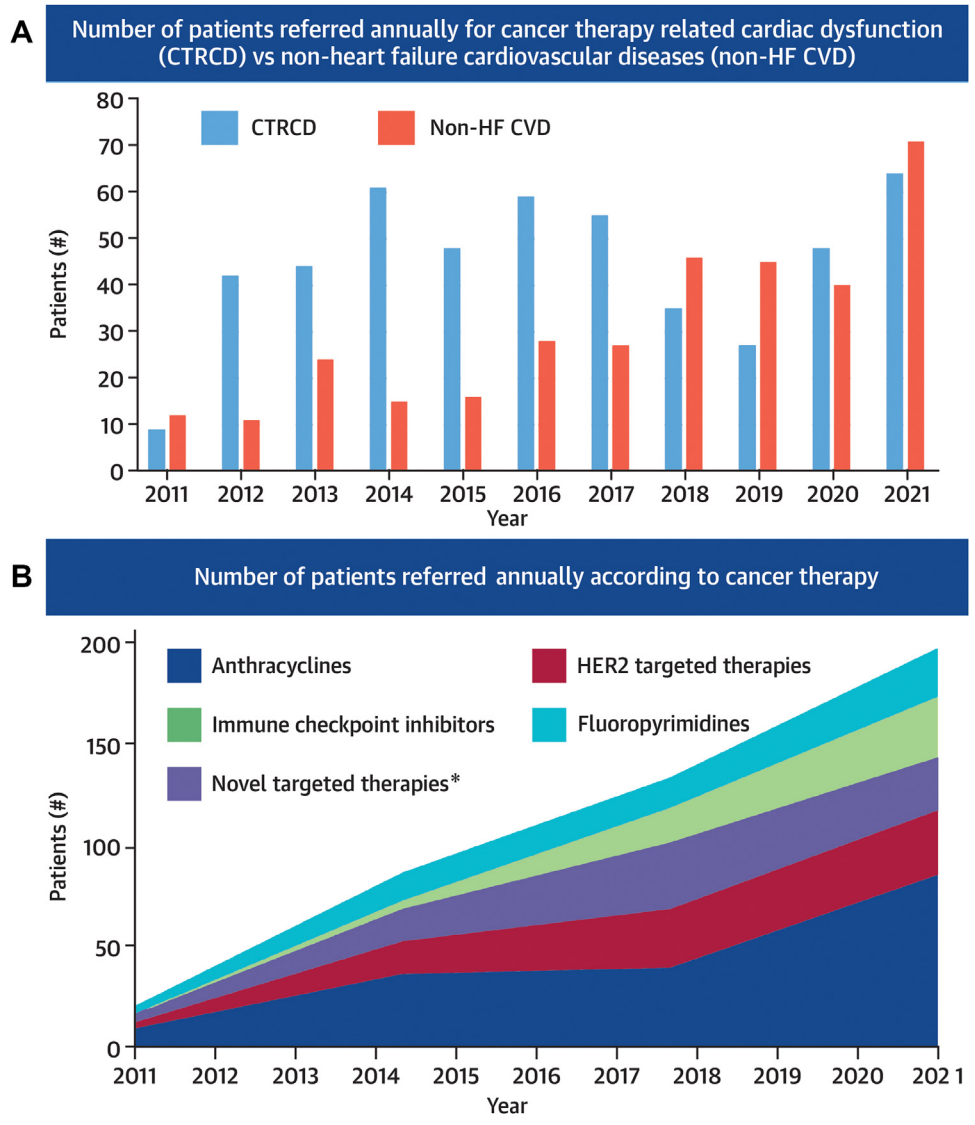
FIGURE 1 **Temporal Trends in Cardio-Oncology Referrals and Pharmacotherapy Utilization (2011-2021)**



(A) The number of patients referred for cancer therapy–related cardiac dysfunction (CTRCD) vs non–heart failure cardiovascular disease (non-HF CVD). (B) The number of patients referred to the cardio-oncology service on different oncology agents along a 10-year period. HER2 = human epidermal growth factor receptor 2. *Novel targeted therapies: Tyrosine kinase inhibitors, BRAF/MEK inhibitors, proteosome inhibitors.

fibrosarcoma B-type and mitogen-activated extracellular signal-regulated kinase inhibitors) revealed that anthracyclines and anti-HER2 therapy increased the likelihood of being referred for CTRCD (OR: 2.03; 95% CI: 1.01-4.06; $P = 0.046$ and OR: 6.21; 95% CI: 2.81-13.71; $P < 0.001$, respectively). Conversely, fluoropyrimidines and ICIs increased the risk of non-HF CVD (OR: 4.15; 95% CI: 1.45-11.80; $P = 0.008$ and OR: 7.84; 95% CI: 2.73-22.47; $P < 0.001$).

In this study, we present data from a dynamic cardio-oncology service demonstrating a shift in the types of CVDs referred driven by the emergence of new oncology treatments. The characteristics of the cardio-oncology population underpin the shift from patients primarily treated with anthracyclines or anti-HER2 leading to CTRCD to a more varied population with higher incidences of leukemia, melanoma, thyroid, renal, and lung cancers. This diverse population

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also exhibits an increased number of CV risk factors while undergoing treatment with ICI or TKIs. A significant limitation of the study involves the potential for data loss because of manual entry by different clinicians over time.

To adapt to these developments, the cardio-oncology service underwent numerous modifications. The service, which began with 2 doctors, has expanded over the years, integrating a multidisciplinary team approach. In 2016, a specialized nurse joined the team, followed by a primary care physician and a clinical pharmacist in 2019, contributing to the holistic care provided to the patient. Collaborations with oncology, hematology, and other CV subspecialties have been established, with weekly multidisciplinary team meetings conducted to evaluate new referrals. Additionally, bimonthly meetings focusing on bone marrow transplant survivors are held in conjunction with the hematology and respiratory medicine teams. Emphasizing education, 9 clinical fellows have been trained thus far, and the pursuit of International Cardio-Oncology Society board examination is encouraged. This evolution underscores the dynamic nature of cardio-oncology, addressing the growing and diverse needs of patients. As demonstrated, cardio-oncology has rapidly evolved from its origin, when most referrals were for CTRCD, to a diverse medical specialty encompassing various domains of cardiology. Future cardio-oncology services should reflect this evolution, embracing a dynamic approach and fostering collaboration with oncology-hematology and cardiac subspecialities as needed.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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