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REVIEW

Radiotherapy-induced right ventricular remodelling: The missing piece of the puzzle

Remodelage ventriculaire droit postradiothérapie : la pièce manquante du puzzle

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Summary The number of studies demonstrating that right ventricular structure, function and mechanics are valuable predictors of cardiovascular and total morbidity and mortality in patients with a wide range of cardiovascular conditions is constantly increasing. Most studies that evaluated the influence of radiotherapy on the heart focused on left ventricular remodelling, which is why current guidelines only recommend detailed assessment of the left ventricle. Data regarding right ventricular changes in cancer patients treated with radiotherapy are scarce. Given that radiotherapy more often induces late cardiac impairment — unlike chemotherapy-induced cardiotoxicity, which is usually acute — it is quite reasonable to follow these patients echocardiographically for a long time (even for 20 years after initiation of radiotherapy). Investigations that have followed cancer survivors for at least 10 years after radiotherapy agree that right ventricular structure, systolic/diastolic function and mechanics are significantly impaired. The mechanisms of radiation-induced right ventricular remodelling

Abbreviations: FAC, fractional area change; LV, left ventricle/ventricular; RIHD, radiotherapy-induced heart disease; RV, right ventricle/ventricular; TAPSE, tricuspid annular plane systolic excursion.

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are still unclear, but it is thought that fibrosis is the dominant factor in myocardial remodelling and vascular changes. Many factors may contribute to right ventricular impairment during and after radiotherapy: cumulative radiation dose; dose per treatment; delivery technique; radiation target (chest and mediastinum); and co-morbidities. In this review, we aim to provide a comprehensive overview of the potential mechanisms of radiation-induced right ventricular remodelling, and to summarize clinical studies involving radiotherapy-treated cancer patients.

MOTS CLÉS
Radiothérapie ;
Cancer ;
Ventricule droit

Résumé Les études ayant rapporté une valeur prédictive forte de la dysfonction ventriculaire droite sur la morbi-mortalité sont en nombre croissant dans la littérature. La majorité des études évaluant l'influence de la radiothérapie sur la fonction cardiaque ont été focalisées sur le remodelage ventriculaire gauche, raison pour laquelle les recommandations actuelles recommandent une évaluation détaillée des dimensions et de la fonction ventriculaire gauche. Les données concernant l'impact d'une radiothérapie chez des patients porteurs d'un cancer sur la fonction ventriculaire droite sont peu nombreuses. En prenant en considération le fait que la radiothérapie induit plus souvent une cardiotoxicité tardive, comparativement à la toxicité aiguë induite par les chimiothérapies anti-cancéreuses, il est raisonnable d'évaluer de façon prospective par échocardiographie au long cours les patients ayant eu une radiothérapie, jusqu'à 20 ans après ce traitement. Les études ayant évalué et suivi des patients porteurs d'un cancer ayant une ancienneté > 2 ans au décours de la radiothérapie concluent tant la structure que la fonction systolique et diastolique ventriculaire droite ainsi que la mécanique ventriculaire droite sont altérées de façon significative au décours d'une radiothérapie. Les mécanismes du remodelage ventriculaire droit induits par la radiothérapie sont inconnus mais il est considéré que la fibrose est le facteur prédominant du remodelage myocardique et des modifications vasculaires. De nombreux facteurs pourraient contribuer à l'altération du ventricule droit pendant et au décours d'une radiothérapie : la dose cumulée, la dose utilisée, les techniques d'administration, la cible de la radiation thorax ou médiastin, ainsi que les comorbidités sont autant de facteurs mis en avant dans les différentes études. Cette revue générale apporte un éclairage sur les mécanismes potentiels du remodelage ventriculaire droit induits par une radiothérapie et résume les études cliniques dans ce domaine.

Background

The number of patients with cancer is increasing each year. However, the modern therapeutic approach, which includes sophisticated chemotherapeutic agents and radiotherapy, has improved survival significantly in these patients. It is estimated that more than 50% of modern anticancer protocols involve radiotherapy. The effect of radiation on different tissues and organs that were not the target of radiotherapy has been recognized for more than 60 years, and it is well known that this effect depends on total amount of radiation, dose per treatment, delivery technique, tissue type and co-morbidities [1,2]. Radiotherapy-induced heart disease (RIHD) typically occurs in patients with Hodgkin's disease, breast cancer (particularly the left breast), lung cancer and other mediastinal malignancies (e.g. oesophageal carcinoma) who have undergone radiotherapy as part of their anticancer treatment. RIHD is associated with vascular, valvular, pericardial, conduction and myocardial damage. The changes in RIHD vary from mild (asymptomatic cardiac impairment) to severe (severe valve disease or symptomatic heart failure).

The mechanisms that are responsible for radiotherapy-induced heart remodelling (i.e. cardiomyopathy, valvulopathy and coronary artery disease) are still unclear. It is known that a cumulative radiotherapy dose of > 30 Gy, irrespective of cancer type, is related to cardiac damage [3]. Given that the contemporary radiotherapy dose for breast cancer is 45—50 Gy [4], and for Hodgkin's lymphoma is 35 Gy [5], it is clear why cardiac assessment should be a mandatory part of the routine evaluation of patients with cancer. Furthermore, the majority of patients with cancer are treated not only with radiotherapy, but also with chemotherapy, which is known to be a strong independent predictor of adverse cardiac remodelling, further increasing the necessity for careful cardiac assessment of patients with cancer.

The primary focus of investigations into RIHD has been the left ventricle (LV) [3,6], which is why current guidelines regarding cancer treatment and cardiovascular toxicity concentrate mainly on left ventricular (LV) assessment [7,8].

Data regarding radiotherapy-induced right ventricular (RV) remodelling are scarce and, in most studies, patients were also treated with chemotherapy, which makes the