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The Role of Echocardiography in Cardio-oncology Patients: Contemporary Indications and Future Directions

心臟超音波於心血管腫瘤領域的當代應用及未來展望

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王晨旭醫師 秦志輝主任摘譯 / 國泰醫院心血管中心一般心臟醫學科

近年癌症檢測及治療有相當進展，死亡率顯著降低，但其療程的 **adverse effect** 仍降低癌症存活率及生活品質。因此，當代癌症治療趨勢已轉向針對 **cancer therapeutics related cardiac dysfunction (CTRCD)** 進行預防、檢測及處置。心血管疾病是目前癌症病人罹病及死亡的第二大主因。CTRCD 的 **cardiotoxicity** 可經 **chemotherapy (CT)**, **radiotherapy (RT)** 的直接毒性誘發，進而出現各種 **cardiac dysfunction (CD)** 臨床症狀。CTRCD 與種種不良預後高度相關，包括心臟移植、心室輔助器置放、甚至死亡。

過去已發現許多 CT 藥物可能導致 CTRCD，尤其 **anthracyclines**, **trastuzumab**, **tyrosine kinase inhibitors & vascular endothelial growth factor inhibitors** 等。RT 也可立即或於曝露數年後誘發 CD。可能源自 CT/RT 對心肌結構/心臟功能的直接影響，或是加速既存的心血管疾病惡化。癌症本身也可誘發 **cardiac remodeling**，換言之，原本因高齡等退化因素造成的 CD，可

能因後續的 CT/RT 進一步惡化。

因此，識別高危險族群並預防 CD、及早發現/治療 CTRCD，已成 **cardio-oncology** 當代顯學。**Trans-thoracic echocardiography (TTE)**，在 **cardiotoxicity** 的偵測/治療尤其重要 (圖 1)。相對於其他影像檢查，TTE 是最容易取得、最廣泛使用、相對安全且具成本效益的臨床工具 (表 1)。

Echocardiography 應用於 cardio-oncology 的臨床指標

(1) Left ventricular (LV) systolic dysfunction (SD)

LV ejection fraction (LVEF) 作為偵測 CD 指標已超過 30 年，目前仍是評估 CTRCD 最廣泛接受的指標之一。以乳癌病人為例，CT 後追蹤 3 年，LVEF 平均可下降 2.8~3.8% (LVEF \geq 55% 視為正常)。European Society of Cardiology (ESC) 定義 CTRCD 為：經 TTE 發現 LVEF $<$ 53%，或經 **multi-gated acquisition scan** 的 **cardiac MRI** 發現 LVEF $<$ 50%；在 2~3 週後重複上述檢查，發現

Fig. 1 Role of echocardiography in cardio-oncology. The figure illustrates the typically journey of a cancer patient undergoing treatment. The utility of echocardiography in the management of the cardiac sequelae of cancer therapy is illustrated by the heart icons and briefly summarised in the corresponding text boxes.

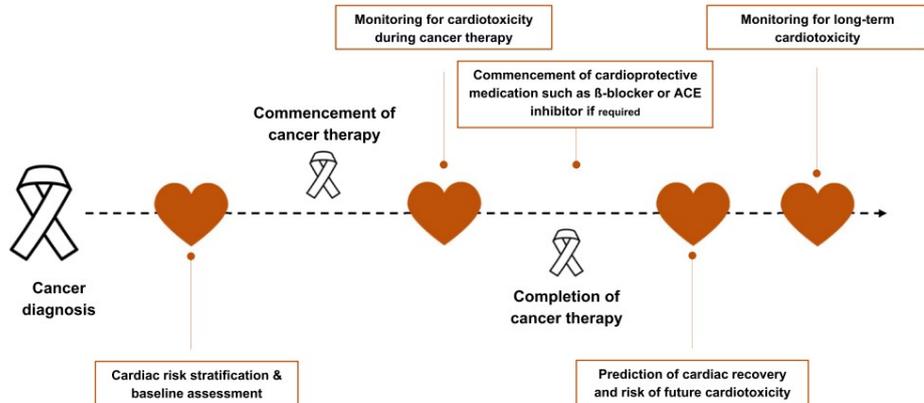


Table 1 Benefits and limitations of the various cardiac imaging modalities used in cardio-oncology

Imaging modality	Benefits	Limitations
Echocardiography	Availability, ease of use, cost-effectiveness, and reproducibility. No radiation exposure. Safe in patients with concomitant renal disease. Allows evaluation of cardiac structure (heart chambers, valves, and pericardium) and haemodynamic function (stroke volume, LV filling pressure, and pulmonary artery pressure) [14••, 15•, 16].	
Cardiac MRI	Reference standard for EF measurement [17]. Allows evaluation of the pericardium and detection of scarring and myocardial fibrosis [5••]. Allows assessment of tissue characterisation, evaluation of cardiac masses, and identification of infiltrative diseases [5••]. No radiation exposure.	Expensive. Limited availability. Use dependent on patient compliance while in scanner.
Multigated acquisition scintigraphy	Longest established method for quantifying LVEF in cancer patients. Robust method to assess LVEF in patients with atrial fibrillation. Superior to 2D echocardiography; values obtained have better correlation with other 3D imaging modalities such as 3D echocardiography and cardiac MRI [14••, 18].	Radiation exposure. Limited ability to assess cardiac structure and haemodynamics [19••]. Inability to measure strain.
Coronary CTA	Useful in patients with chest pain and prior chest irradiation to assess coronary artery disease.	Radiation exposure. Not used routinely to assess LVEF.

EF, ejection fraction; LVEF, left ventricular ejection fraction; MRI, magnetic resonance imaging; CTA, computed tomography angiography

表一

LVEF 降低>10%，得以確診。LV volume 及 LVEF 的定量可使用 2D TTE (2D)的 modified biplane Simpson' s technique。3D TTE (3D)量測 LVEF 比 2D 更精準，誤差<5% (2D 誤差>10%)。但臨床上 3D 不若 2D 廣泛方便使用，且目前仍缺乏 3D 對 CTRCD 診斷有改善的研究。運用 myocardial contrast agents 可更清楚描繪 endocardial border，LVEF 也可與 wall motion score index 相結合計算。

(2) Global longitudinal strain (GLS)

LVEF 取決於血流動力學，敏感性不若 myocardial deformation。Myocardial deformation (strain)的測量可利用 Doppler tissue imaging (DTI) 或 2D speckle tracking echocardiography (STE)。透過 2D STE GLS，計算 LV 收縮變形程度進而反映 SD。在 2D LVEF 明顯降低前，GLS 通常已惡化。若 CT 後的 GLS 相對 baseline (CT 前)下降>15%，可能發生 CTRCD；若 GLS 相對 baseline 降低<8%，目前認為無臨床意義。GLS 具良好 intra-及 inter-observer reproducibility，並與 CT (anthracycline≥250 mg/m²)累積劑量以及 RT 相關性良好。GLS 可用於 CTRCD 出現 subclinical LV dysfunction 的偵測。

(3) LV diastolic dysfunction (DD)

LV 舒張功能評估，包括 grading of diastolic

function 及 estimate of LV filling pressures。利用 E/e' ，即 mitral peak velocity of early filling (E) 及 early diastolic mitral annular velocity (e')的比值，若用來比較乳癌病人 CT 前後 3 個月 LV 功能變化，可發現 DD 比 SD 平均提早 73 天出現，同時期 LVEF 變化值可能尚不足量測到 SD。亦即 E/e' 變化比 LVEF 更能早期檢測 LV dysfunction。傳統 DD 指標(mitral inflow analysis & LA volume/function)在乳癌族群經 6 週 RT 雖無變化，但 diastolic strain (E-Sr & A-Sr)這類指標已見明顯下降。同研究在 GLS 降低>10%的病人群組中，傳統 DD 指標和 diastolic strain 指標都有更大幅度的降低，顯示上述指標尤其 diastolic strain 可早期預測 CD。近期有研究嘗試探討 DD 指標 (mitral E, lateral E' & mitral E/A)在預測 CTRCD 的有效性。儘管 DD 指標異常可反映 subclinical LV dysfunction，並比 SD 提早出現，但目前 CTRCD 的預後價值和臨床意義仍未完全確定。

(4) Right ventricular (RV) function

RV 功能變化也可早期偵測 CTRCD，因 CT/RT 後 LV/RV 的變形機轉遵循著類似的時間模式/損傷程度。RV GLS 下降>14.8%，可預測發生 CD。但 RV GLS 的 sensitivity/specificity 似乎比 LV GLS 稍差。某肺癌研究經半年 RT+CT 發現，RV free wall strain 及 RV GLS 數值降低，但

Table 2 Factors that increase the risk of cancer therapeutics-related cardiovascular dysfunction

Cancer therapy-related risk factors [16, 57–61]	Patient-related risk factors [16, 62–66]
1. High-dose anthracycline e.g. doxorubicin ≥ 250 mg/m ² or epirubicin ≥ 600 mg/m ²	1. Older age at treatment (≥ 60)
2. High-dose radiotherapy e.g. radiotherapy ≥ 30 Gy with the heart in the treatment field	2. Moderate or severe valvular heart disease
3. Lower-dose anthracycline in combination with lower-dose radiotherapy	3. Hypertension
4. Lower-dose anthracycline or trastuzumab alone in the presence of multiple (≥ 2) cardiovascular risk factors such as smoking, hypertension, diabetes mellitus, dyslipidaemia, and/or obesity	4. History of myocardial infarction
5. Treatment with lower-dose anthracycline (doxorubicin < 250 mg/m ² or epirubicin < 600 mg/m ²) followed by trastuzumab	5. Compromised cardiac function e.g. LVEF 50–55%
6. Autologous bone marrow transplantation.	

LVEF, left ventricular ejection fraction

表二

因追蹤時間過短及與 LVEF 相關性不明，臨床意義有限。目前 RV 功能量測對 CTRCD 的臨床意義仍待驗證。

(5) 其他 echocardiography 指標

其他指標包括 LV torsion, longitudinal peak systolic strain, circumferential strain, intraventricular pressure gradient, left atrial volume, cyclic variation of integrated backscatter & ventricular-arterial coupling 等，在 CT/RT 後可能變化。但目前上述指標與 LVEF 下降間的相關性及長期預後價值尚未建立，臨床意義仍不確定。近年研究包括：乳癌 CT 後追蹤 4~6 個月 radial strain 的變化，與追蹤 2 年時的 LVEF 變化顯著相關。Circumferential strain 的早期惡化，與 CT 後 1 年時的 LVEF 下降 2% 顯著相關，並在追蹤 2 年時的 LVEF 下降變化達到統計學上顯著意義。CT/RT 後 6 個月，longitudinal peak systolic strain 的 0.1/s 比值惡化與追蹤 12 個月時的 CTRCD 相關。Relative wall thickness 的減少、E/a & end-systolic stress 的早期增加，與追蹤 1 年時 LVEF 的下降有顯著相關，但比較追蹤 2 年時卻無統計意義。另一研究，LV segmental wall motion abnormality 被證明是與 GLS 一致的 CTRCD 預測指標。Prolongation of LV electromechanical delay：計算 ECG 的 QRS onset 到 pulsed-waved Doppler echocardiography 的 trans-aortic flow peak 的 time interval 延長，可能是 CD 另一個早期預測指標，這種 time interval 延長早於 LVEF 和 GLS 變化前。以上種種指標，目前均尚未應用於臨床。

Echocardiography 在 cardio-oncology 中的角色

(1) 癌症病人風險分級及 baseline 心臟功能評估

癌症病人比非罹癌族群有更高的心血管疾病罹病及死亡率。表 2 整理 CTRCD 高風險療程及高風險病人特徵。Echocardiography 能針對準備接受 CT/RT 病人進行風險分級及 baseline 心臟功能評估。建議 CT/RT 前評估 echocardiography 指標(如 LVEF & GLS)及生物標記(如 troponin)。心臟/腫瘤科醫師應一同根據癌症病人 baseline 心臟功能風險、CT/RT 配方類型/劑量以及職業/環境等後勤因素，討論癌症病人後續追蹤時程。將心血管危險因子以及既存的 CD 積極改善，將有助降低後續 CTRCD 的風險。包括改善三高、戒菸、減重以及適量運動等。儘管早期篩檢出高危險病人有其益處，但目前研究也發現醫療單位對於接受 RT 的病人進行 CD 篩檢必要性的認知仍然偏低。因此，在缺乏心臟專科醫師的癌症中心，提高醫療人員對接受 CT/RT 病人的 CD 風險認知可能是有益的。

(2) 癌症療程期間以及療程後的臨床監測

有症狀的癌症病人，在 CT/RT 期間以及療程完成後，應進行週期性的 TTE 心臟功能評估。過去在乳癌的研究發現，無論 baseline LVEF 好壞，CT 後 3 個月內 LVEF 就下降 $\geq 5\%$ ；中位數追蹤 4.5 年就會發生 CTRCD。CT (anthracycline ≤ 240 g/m²) 累積劑量低風險病人，在完成療程及療程後 6 個月應 TTE 再評估。若 CT 累積劑量超過上述，後續每增加 50 mg/m²，隨後每個療程前應 TTE 再評估。準備進行 CT 的病人若過去曾接受

Table 3 Current guidelines for the role of echocardiography in the management of CTRCD. Recommendations are in accordance with the ASCO, ESC, CCS, and ESMO guidelines as indicated

Signs	Recommendation	Organisation
Anthracycline-induced toxicity		
1. Decline in LVEF ≥ 10 to $< 50\%$	Repeat assessment of LVEF [5••]. Commence ACE inhibitor (or ARB) and β -blocker to prevent further LV dysfunction [5••].	ESC
3. Symptomatic LV dysfunction (LVEF $< 40\%$)	Cease chemotherapy and commence appropriate heart failure therapy with ACE inhibitor (or ARBs) and β -blockers [19••].	ESMO
4. LVEF is $> 40\%$ but $< 50\%$	Reassess cardiac function in 3 weeks. If this is confirmed, cease chemotherapy and commence appropriate heart failure therapy and more frequent follow-up [19••].	ESMO
5. Symptomatic heart failure without a decline in LVEF	Chemotherapy can be continued [19••].	ESMO
6. Asymptomatic decline in LVEF to $< 40\%$ or an LVEF reduction of $\geq 15\%$ from baseline to $< 50\%$	Withhold cancer therapy, commence heart failure therapy, and discuss with the cardio-oncology team [19••].	ESMO
7. Asymptomatic decline in LVEF to $< 50\%$ but greater than 40%	Cancer therapy can be continued. Commence ACE inhibitor (or ARB) and β -blocker plus more frequent echocardiography and clinical review [19••].	ESMO
8. Troponin positive patients	Start ACE inhibitor to prevent decline in LVEF and do an echocardiogram at the end of the cancer therapy and 3-monthly thereafter [19••].	ESMO
Trastuzumab-induced cardiotoxicity		
1. Decline in LVEF to $< 45\%$ or by $> 10\%$ from baseline to a value between 45 and 49%	Withhold trastuzumab and repeat LVEF measurement in 3 weeks [5••, 15•, 16]. If the LVEF is restored to $> 49\%$, trastuzumab may be reinitiated [5••, 15•, 16]. If the LVEF remains between 45 and 49% , trastuzumab may be continued but an ACE inhibitor should be initiated [5••, 15•, 16]. If the LVEF remains $\leq 44\%$, cease trastuzumab and commence ACE inhibitor and β -blocker [5••, 15•, 16].	ASCO, CCS, ESC
2. Symptomatic heart failure	Commence ACE inhibitor (or ARB) and β -blocker [19••].	ESMO
3. Asymptomatic decline in LVEF to $< 40\%$	Commence ACE inhibitor (or ARB) and β -blocker. ACE inhibitors alone are sufficient for asymptomatic patients, however in the setting of a previous myocardial infarction, β -blocker may be added [19••].	ESMO
4. Symptomatic heart failure with LVEF between 40 and 50%	Consider commencing ACE inhibitors [19••].	ESMO

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; ASCO, American Society of Clinical Oncology; ASE, American Society of Echocardiography; CCS, Canadian Cardiovascular Society; CTRCD, cancer chemotherapeutics-related cardiac dysfunction; ESC, European Society of Cardiology; ESMO, European Society of Medical Oncology

表三

CT 或在心臟區域接受過 RT，應於療程期間每 3 個月和療程完成後重新一次 TTE 再評估。若病人出現 CD 症狀、影像學出現任何異常或發現 troponin 升高，均應 2 週內重複進行 TTE 並接受心臟專科進一步諮詢以利確診。

具高風險 CTRCD 的無症狀癌症病人，建議療程完成後 6~12 個月內進行 TTE。若檢查時影像學上未出現 CD，則依臨床病況進一步安排後續影像檢查。若發現任何影像學異常或 CD 症狀惡化，應進一步評估並進行心臟專科諮詢。接受高劑量胸部 RT (> 30 Gy) 應考慮在初次 RT 後 10~15 年進行 TTE，之後每 5 年追蹤。

American Society of Echocardiography (ASE) 及 European Association of Cardiovascular

Imaging (EACVI) 建議將 MRI 作為心臟影像檢查的另一選擇，當出現 CTRCD 終止療程或改變 CT 配方、TTE 成像困難且無法經對比劑增強判讀結果，需要精準的組織特徵顯像等。Multi-gated acquisition scan 也常用來作為 TTE 的輔助而非替代檢查，尤其 TTE 技術上不可行或臨床上無法使用時。

(3) Echocardiography 及生物標記檢查

根據 European Society for Medical Oncology (ESMO) 指引，目前透過兩種方案對 CTRCD 進行追蹤監測。方案一僅用心臟成像；方案二結合 serum troponin 和心臟成像，在 baseline 心臟功能評估及 TTE 完成後定期安排追蹤。方案一，TTE 定期在 CT 療程前、療程間的第 3、6、9 個月，

Table 4 A summary of recommendations for the diagnosis, monitoring, treatment, and follow-up of CTRCD. The type and strength of evidence behind the recommendation is created by ASCO using the GuideLines Into Decision Support (GLIDES) methodology. The strength of each

recommendation is rated as strong, medium, or weak based on the evidence of a true net effect, consistency of results, concerns about study quality and the extent of agreement among panellists [16]

Recommendation	Organisation	Type	Strength
1. Echocardiography is the standard imaging modality of choice for assessment of cardiac structure and function.	ASE/EACVI	Evidence-based	Strong
2. If echocardiography is not available or technically feasible, a multigated acquisition scan or cardiac MRI can be used, with preference given to cardiac MRI.	ASCO, ASE/EACVI	Evidence-based	Moderate
3. The same imaging modality and method should be utilised to determine LVEF before, during, and after completion of cancer therapy.	CCS, ASE/EACVI	Formal consensus	Moderate
4. 3D echocardiography is the preferred imaging technique in monitoring LV function and detecting CTRCD.	CCS, ASE/EACVI	Formal consensus	Moderate
5. 2D STE (GLS) and serum biomarkers, in particular troponin, are useful tools for detecting subclinical LV dysfunction but its significance is still unknown.	ESC, ASCO, CCS, ASE/EACVI, ESMO	Formal consensus	Moderate
6. Evaluation of LVEF prior to commencement of potentially cardiotoxic cancer treatment is necessary. Periodic assessment during and post treatment is recommended especially in symptomatic patients.	ESC, ASCO, CCS, ASE/EACVI, ESMO	Formal consensus	Strong
7. Baseline evaluation of LVEF, GLS, and troponin should be undertaken prior to initiation of agents associated with CTRCD.	ESC, ASCO, CCS, ASE/EACVI	Evidence-based	Moderate
8. Serial assessments with cardiac imaging and/or serum biomarkers are recommended during treatment and post completion of therapy.	ESC, ASCO, CCS, ASE/EACVI, ESMO	Evidence-based	Moderate
9. In patients who receive high doses of chest irradiation, screening with non-invasive imaging should be considered 10 to 15 years after the initial treatment.	ESC, ASE/EACVI	Evidence-based	Weak
10. Significant changes in LVEF necessitate confirmation with repeat imaging within 2 to 3 weeks. A significant decline in LVEF warrants initiation of heart failure treatment (ACE inhibitors/ARBs and beta blockers).	ESC, ASCO, CCS, ESMO	Evidence-based	Strong
11. The decision to withhold or discontinue cancer therapy should be made by the oncologist in close collaboration with a cardiologist after considering the risks and benefits of continuation of therapy.	ASCO	Informal consensus	Weak

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; ASCO, American Society of Clinical Oncology; ASE, American Society of Echocardiography; CCS, Canadian Cardiovascular Society; CTRCD, cancer chemotherapeutics-related cardiac dysfunction; EACVI, European Association of Cardiovascular Imaging; ESC, European Society of Cardiology; ESMO, European Society of Medical Oncology; GLE, global longitudinal strain; LV, left ventricle; LVEF, left ventricular ejection fraction; MRI, magnetic resonance imaging; STE, speckle tracking echocardiography

表四

以及療程開始後的第 12、18 個月進行追蹤。方案二，在每個 CT 療程後定期評估 serum troponin。若 serum troponin 持續陰性，仍建議每年度進行 TTE。目前證據顯示，雖然 CT 後 troponin I/troponin T 可能已上升，但與心臟功能變化間的關聯尚不明確。且 troponin T >0.008 ng/mL 的 positive predictive value (PPV) 僅 54.5 % 偏低。目前由於證據仍不足，troponin 用來監測 CTRCD 仍應謹慎使用。

(4) Cardiotoxicity 的初級防護及治療

開始 CT 前，預防性投與 β blockers (ex: carvedilol) 與降低 CD、減少 troponin 上升有關。但投與 β blockers 對於無症狀的 LVEF 下降、brain natriuretic peptide (BNP) 變化、all-cause mortality，目前無證據有相關性。投與 ACE inhibitor (ex: lisinopril) 在接受 CT 乳癌病人上，與 carvedilol 同樣有效減少 CTRCD 及中斷 CT 發生

率。以上兩種保護性藥物，CT 後追蹤 12 個月，均未影響病人生活品質。許多指引顯示(表 3) 早期發現 CTRCD 是心血管良好預後的關鍵，TTE 扮演著關鍵角色。若影像追蹤發現 LV dysfunction，應改變/終止療程配方、投與心臟保護藥物、並訂定追蹤監測時程。儘早治療 CD，對 CTRCD 病人有益。

Echocardiography 在 cardio-oncology 中的臨床限制

與其他影像檢查工具相較(表 4)，echocardiography 具備許多優點。但其量測值 reproducibility 及缺乏 standardization of measurement conventions 仍是存在已久的問題。另有研究發現許多 echocardiography 指標對心臟功能長期預測能力有限。GLS 作為 CTRCD 早期預測指標也受到質疑，未來仍需進一步研究證實 GLS 監測 subclinical CTRCD 的臨床實用性。

Table 5 Cardiac imaging parameters and circulating biomarkers being investigated as predictors of early cardiotoxicity in the EARLY HEART study. Table modified from Walker et al. [93]

2D STE	
<ul style="list-style-type: none"> • Global and segmental longitudinal strain and strain rate • Global and segmental radial strain and strain rate • LVEF using Simpson's biplane method • E/A wave ratio: ratio of peak velocity blood flow from gravity in early diastole (the E wave) to peak velocity flow in late diastole caused by atrial contraction (the A wave) • E/Ea wave ratio: ratio of peak velocity blood flow from gravity in early diastole (the E wave) to early diastolic velocity of lateral mitral annulus (e' lateral) • Tricuspid annular plane systolic excursion • Heart rate • Cardiac output measured by multiplying heart rate by the stroke volume 	
Computed tomography coronary angiography	
<ul style="list-style-type: none"> • Coronary artery calcium score, overall and per artery • Presence and type of plaque (noncalcified, partly calcified, and calcified); overall and per segment or artery • Presence and severity of luminal narrowing based on plaque; overall and per segment or artery 	
Magnetic resonance imaging	
<ul style="list-style-type: none"> • RV end-diastolic and end-systolic volumes, LV end-diastolic and end-systolic volumes, LV mass • LVEF, RVEF • Presence and extent of myocardial infarction based on delayed enhancement • Tissue characterisation based on pre- or postcontrast T1 mapping • Presence of myocardial oedema based on T2 mapping 	
Circulating biomarkers	
<ul style="list-style-type: none"> • Markers of cardiac injury: CRP, Troponin I, Troponin T, BNP, N-terminal-proBNP, beta2-microglobulin, Galectin 3 • Extracellular vesicles: CD14 (monocytes), CD31 (endothelial), CD41 (platelets), CD3 (lymphocytes), CD235a (erythrocytes); exosomes • Cardiac miRNAs (miR-1, miR-24, miR-133a/b, miR-208a/b, miR-210); non-cardiovascular miR-122 • Circulating DNA methylation 	
<p><i>BNP</i>, B-type natriuretic peptide; <i>LVEF</i>, left ventricular ejection fraction; <i>RVEF</i>, right ventricular ejection fraction; <i>CRP</i>, C-reactive protein</p>	

表五

Echocardiography 在 cardio-oncology 中的未來展望

(1) Echocardiography 檢查結果的 Validation

儘管許多 echocardiography 指標似乎可用於 subclinical CTRCD 早期檢測，但臨床價值尚未得到驗證。表 5 列出了歐洲近期的 MEDIRAD EARLY HEART 研究，針對乳癌在 RT 後 2 年內發生輻射導致的 CTRCD，進行創新心臟成像指標和循環生物標記的鑑定/驗證。其結果將有助風險分級評估並提供初級/次級防護建議。另有為期 3 年的 SUCCOR 研究，比較 GLS 與傳統 LVEF 作為 CTRCD 指標的臨床角色。初步結果顯示，隨機分配到以 GLS 追蹤的 40 病例中，已有 15 例開始了心臟保護治療，而另以 EF 追蹤的 46 病例中，只有 4 例開始相同的治療。目前兒科癌症病童仍使用類似成人的 CTRCD 風險評估方法及早期檢測策略。有研究利用過去偵測早期 cardiac

re-modeling 的工具，如 LV wall thickness Z-score & LV thickness-to-dimension ratio，嘗試作為未來兒科病童 CT 後追蹤 LV global dysfunction 的預測指標。

(2) Echocardiography 結合其他檢查工具的臨床應用

其他心臟功能檢查可強化 echocardiography 的臨床判讀能力。一項針對童年癌症經 CT 後的成年存活病人之回溯研究發現 QTc prolongation 與 subsequent LV dysfunction 間有相關性。與正常病人相較，出現 LV dysfunction 病人其 QTc 比前者更長(451±32 ms vs. 423±25 ms)。從 ECG 出現 QTc≥450 ms 到 TTE 發現 LV dysfunction 平均為 1.8±2.9 年。對 CT/RT 病人進行 QT interval 監測可能有效，但目前 ECG 異常與 TTE 對 CD 證據一致性仍偏低。

研究發現，Portable Wireless Devices (PWD) 同步搜集 carotid arterial pulse waveform & phonocardiogram data 得到的 LVEF 比 TTE 更為準確，與運用 MRI 量測 LVEF 的黃金標準相當。且 LVEF 的相關性比較中，PWD vs MRI (R=0.44) 高於 TTE vs MRI (R=0.12)。以 MRI 為參考值，PWD 具有 high sensitivity & low false-negative rate。未來通過認證，PWD 技術即可應用於初級篩檢，不會在成像和判讀結果間存在著時間延遲。

18 Fluorodeoxyglucose positron emission tomography (18FDG-PET) 在 CT 後 1 週內就可觀察到 RV wall glucose metabolism 增加。研究發現 CT 後 LV glucose uptake 顯著增加，而 TTE LVEF 並無任何變化。CT 前後 LVEF 變化與 LV 標準化

glucose uptake 數值呈負相關，LV 標準化 glucose uptake 高於中位數的病人之 LVEF 也明顯降低。18FDG-PET 結合 TTE 可能是 CT/RT 後早期心臟監測的有效工具，但目前常規使用 18FDG-PET 可能因保險及不同專科需求而受限。

Artificial Intelligence (AI) 及 Machine Learning (ML) 的優點在於自動化的擷取和影像的判讀。最近已啟用全自動具延伸性的 AI/ML 管道，開始進行圖像分類、影像分割、心臟結構功能測量以及疾病檢測。自動化 echocardiography 檢查，以監測 CTRCD，進而改變治療策略，為無症狀 CD 早期檢測提供了具經濟效益的前景。未來可提高病人時序性追蹤的頻率，其中大部分可在基層醫療機構中完成。