



Cardio-Oncology at the Point of Referral: Who Needs Baseline Imaging and Who Does Not

Annelie Wenger-Baumann^{1*}, Ciaran Kinsella-Byrne², Sylwia Radomska³

¹Department of Cardio-Oncology, Limmat Institute of Cardiovascular Medicine, Zurich, Switzerland

²Department of Medical Oncology, Dodder Institute of Cardiovascular Medicine, Dun Laoghaire, Ireland

³Department of Cardiovascular Imaging, Sudety Heart Centre, Walbrzych, Poland

*Correspondence to: Annelie Wenger-Baumann, Department of Cardio-Oncology, Limmat Institute of Cardiovascular Medicine, Zurich, Switzerland

E-mail: a.wengerbaumann@licm.ch

Received: 20 January 2022; Accepted: 13 May 2022; Published: 17 August 2022

Copyright: © 2022 Wenger-Baumann A, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Guidelines answer the question of who needs baseline cardiac assessment before potentially cardiotoxic cancer therapy with a specific tool: the HFA-ICOS risk stratification framework, which sorts patients into low, moderate, high, or very-high risk categories and recommends escalating baseline echocardiography, biomarker testing, and cardiology referral accordingly. The 2022 ESC Cardio-Oncology Guidelines endorse this approach with Class I recommendations, and a meta-analysis of unselected breast cancer patients receiving anthracyclines found that routine baseline assessment has genuinely low yield -- only 2.5% of patients showed an abnormal baseline left ventricular ejection fraction, and only 1.6% had their chemotherapy decision changed as a result -- supporting the case for a risk-stratified rather than universal approach. But a real-world validation of the HFA-ICOS tool in 687 HER2-positive breast cancer patients found that the tool the guidelines rely on to decide who is low risk and who is not barely distinguishes them in practice: composite cardiotoxicity occurred in 38.8% of patients labelled low risk, 38.5% of those labelled moderate risk, and 41.4% of those labelled high risk -- a nearly flat curve, with area-under-curve discrimination of only 0.51-0.55 across outcome definitions, barely better than chance. Only the very-high-risk category, containing just 4 of the 687 patients, showed a clearly different event rate. This review sets out the guideline framework for baseline risk stratification, the evidence supporting a selective rather than universal approach to baseline imaging, and the complication those two positions run into when they meet: a risk tool that is genuinely useful for excusing the truly low-yield majority from unnecessary testing is far less reliable, on current evidence, for confidently telling any individual low-risk patient that their personal risk of cardiotoxicity is actually lower than a moderate- or high-risk patient's.

Keywords: Cardio-oncology; Baseline risk assessment; HFA-ICOS; Cardiotoxicity; Cancer therapy-related cardiac dysfunction

Introduction

Cancer therapy has grown steadily more effective and, for a meaningful subset of drug classes, steadily more cardiotoxic: anthracyclines, HER2-targeted agents, and a growing list of other compounds can injure the heart in ways ranging from asymptomatic decline in ejection fraction to overt heart failure. The oncologist referring a patient for cardiology input at the

point of treatment decision faces a concrete question with a guideline-endorsed answer: stratify the patient's baseline cardiovascular risk using a validated tool, and let that stratification decide how much baseline testing -- echocardiography, biomarkers, cardiology referral -- the patient actually needs [1,2].

This review sets out that guideline framework, the evidence that a selective rather than universal approach to baseline

testing is justified, and a complication that a recent real-world validation study has exposed: the specific tool guidelines use to decide who counts as low risk may not distinguish low-risk from high-risk patients nearly as well as its widespread adoption implies.

Material and Methods

This is a narrative review of the 2022 ESC Cardio-Oncology Guidelines' baseline risk stratification recommendations, the earlier HFA-ICOS position statement those guidelines build on, the meta-analytic evidence on the yield of routine baseline cardiac assessment, and a recent real-world validation study of the HFA-ICOS tool's discriminatory performance, identified through the sources cited above and citation tracking between them, without a pre-registered protocol or systematic search string. All percentages, sample sizes, and performance statistics reported here are taken directly from the cited sources; none has been invented, estimated, or extrapolated.

Results

Guidelines stratify baseline risk into four tiers with escalating recommended testing

The HFA-ICOS tool, endorsed by the 2022 ESC Cardio-Oncology Guidelines, assigns patients starting anthracycline chemotherapy or HER2-targeted therapy to one of four risk categories -- low, moderate, high, or very high -- based on prior cardiovascular disease, cardiovascular risk factors, and prior cardiotoxic exposure [1,2]. Representative criteria escalate the category sharply: no risk factors places a patient in the low tier, while hypertension, chronic kidney disease, diabetes, current smoking, or obesity place them in the moderate tier; prior myocardial infarction, coronary revascularisation, an ejection fraction under 50%, or age 80 or older place them in the high tier; and prior heart failure, cardiomyopathy, or prior cancer therapy-related cardiac dysfunction place them in the very-high tier outright [1]. Figure 1 sets this escalating structure out directly. The guidelines recommend baseline echocardiography with 3D ejection fraction and global longitudinal strain as a Class I recommendation for essentially all patients about to receive these therapies, but reserve baseline biomarker testing -- troponin and natriuretic peptide -- as Class I only for high- and very-high-risk patients, Class IIa (should be considered) for moderate-risk patients, and Class IIb (may be considered) for low-risk patients; cardiology referral is recommended specifically for patients stratified as high or very high risk [1]. In practice, professional-society echo protocols operationalise this into a comprehensive baseline scan before therapy begins, followed by surveillance echocardiography every 3 months during active anthracycline or trastuzumab treatment, with post-treatment surveillance extending 1 to 5 years depending on the patient's risk profile and whether cancer therapy-related cardiac dysfunction actually developed [4].

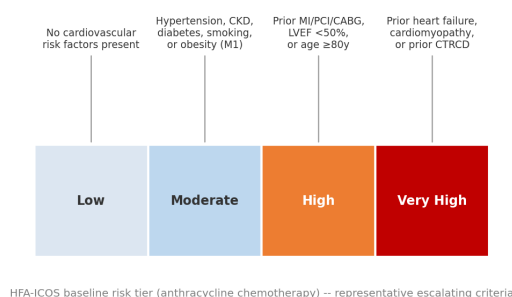


Figure 1: HFA-ICOS baseline risk tier structure for anthracycline chemotherapy, with representative escalating criteria at each tier [1,2].

Routine baseline testing in an unselected population has genuinely low diagnostic yield

The case for stratifying rather than testing everyone the same way rests on more than convenience. A systematic review and meta-analysis pooling eight studies (six of them, totalling 2,545 patients, reporting quantitative findings) found that only 2.5% of unselected early-stage breast cancer patients about to start anthracycline chemotherapy had an abnormal baseline left ventricular ejection fraction, and that baseline assessment changed the chemotherapy decision in only 1.6% of patients overall -- a finding that held regardless of whether echocardiography or MUGA scanning was used [3]. Figure 2 sets these two figures out together. The authors concluded that routine baseline assessment in all early-stage breast cancer patients has low yield, and explicitly called for tools to identify which patients could safely skip it without delaying chemotherapy [3]. This is precisely the gap the HFA-ICOS tool was designed to fill: rather than testing everyone with a low prior probability of an abnormal result, use risk stratification to identify the minority in whom baseline testing is more likely to matter [1,2].

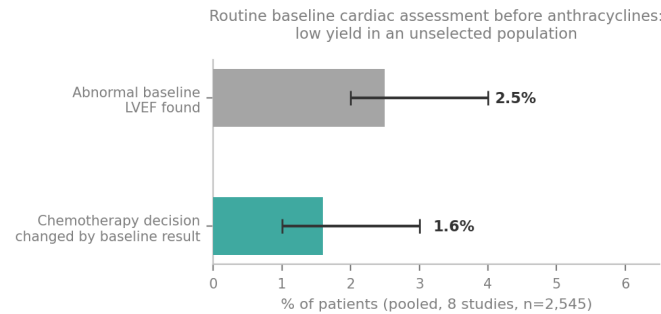


Figure 2: Diagnostic yield of routine baseline cardiac assessment before anthracycline chemotherapy, unselected population, pooled across 8 studies [3].

A real-world validation shows the risk tool barely separates the outcomes it is meant to predict

A 2026 study applied the HFA-ICOS tool to 687 real-world HER2-positive breast cancer patients and followed them for a median of 3.4 years, recording composite cardiotoxicity as well as ejection-fraction-defined, global-longitudinal-strain-defined, and ECG/arrhythmia-defined sub-endpoints separately [6]. Most patients fell into the low (245, 35.7%) or moderate (257, 37.4%) tiers, with 181 (26.4%) classified high risk and only 4 (0.6%) classified very high risk [6]. Figure 3 shows how small that very-high-risk group is relative to the rest of the cohort. The composite cardiotoxicity rate, however, barely moved across the three larger tiers: 38.8% in the low-risk group, 38.5% in the moderate-risk group, and 41.4% in the high-risk group -- essentially indistinguishable from one another -- with only the four very-high-risk patients (all four of whom developed cardiotoxicity) standing clearly apart [6]. Figure 4 sets this pattern out as a heatmap across all four outcome definitions, and Figure 5 overlays the flat rate curve against each tier's very different sample size, making the same point from a different angle: whatever the risk tool is doing, it is not doing it by meaningfully separating low-risk patients' actual outcomes from high-risk patients' actual outcomes.

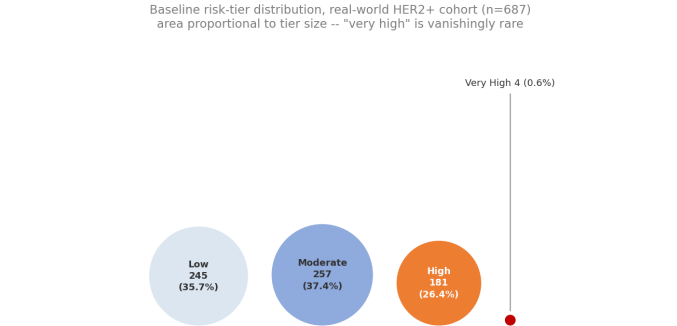


Figure 3: Baseline risk-tier distribution among 687 real-world HER2-positive breast cancer patients; area proportional to tier size [6].

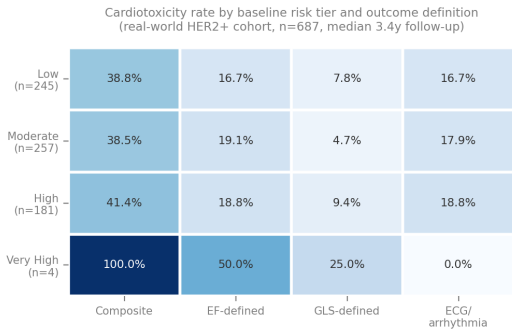


Figure 4: Cardiotoxicity rate by baseline risk tier and outcome definition, real-world HER2-positive breast cancer cohort [6].

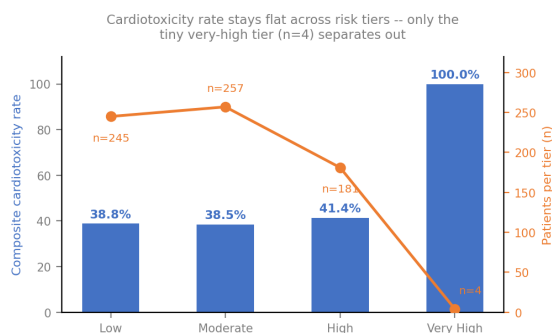


Figure 5: Composite cardiotoxicity rate by risk tier plotted against tier sample size, showing a flat rate curve across markedly different group sizes [6].

The authors quantified this formally: area-under-curve discrimination ranged from only 0.51 to 0.55 across the four outcome definitions -- barely above the 0.50 expected from chance alone -- with sensitivity of 0.28 to 0.37 and specificity of 0.73 to 0.74 [6]. Figure 6 plots these ranges against the 0.50 reference line directly. The authors concluded that baseline HFA-ICOS stratification "showed limited ability to clearly distinguish cardiotoxicity risk across categories" and recommended using the tool to guide surveillance intensity rather than as a standalone predictive instrument, paired with dynamic, on-treatment monitoring rather than reliance on the baseline categorisation alone [6].

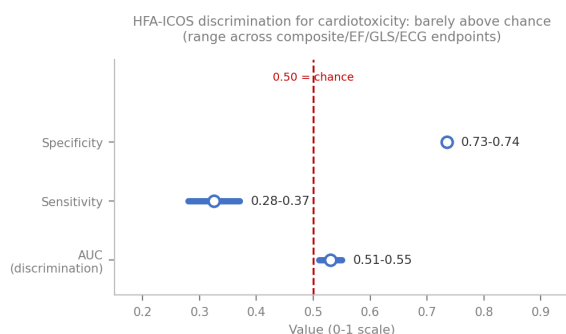


Figure 6: HFA-ICOS discrimination, sensitivity, and specificity for cardiotoxicity, real-world validation across four outcome definitions, against the 0.50 chance reference line [6].

Risk tier (n)	Composite CTx	AUC (all endpoints)
Low (245)	38.8%	0.51-0.55
Moderate (257)	38.5%	0.51-0.55
High (181)	41.4%	0.51-0.55
Very high (4)	100.0%	0.51-0.55

Table 1: Composite cardiotoxicity (CTx) rate by HFA-ICOS tier against the tool's overall discrimination range across outcome definitions [6].

Discussion

Both halves of the evidence reviewed here are, individually, well supported. Routine baseline testing in an unselected population genuinely has low yield: 2.5% abnormal findings and 1.6% practice change is not a rate that justifies universal, resource-intensive baseline echocardiography and biomarker panels for every patient regardless of clinical context [3]. And a validated risk-stratification framework that lets clinicians focus that testing on the patients most likely to need it is, in principle, exactly the right tool for that job [1,2]. The complication is that the specific tool guidelines have adopted for this purpose has now been shown, in a real-world cohort large enough to matter, to barely separate the outcomes it is meant to predict: an area under the curve of 0.51 to 0.55 is close enough to the 0.50 line of no discrimination that a clinician using this tool to reassure a low-risk patient they can skip baseline imaging is relying on a categorisation whose low-risk label carried almost the same cardiotoxicity rate, in this cohort, as the high-risk label [6].

This does not mean baseline risk stratification should be abandoned; it means the confidence placed in any single patient's categorisation should be recalibrated. A sensitivity of 0.28 to 0.37 means the tool misses roughly two-thirds of patients who will actually develop cardiotoxicity when it labels them low or moderate risk, and this is, in this sense, the single most consequential number in this review: it is the number that should give an oncologist or cardiologist pause before treating a "low risk" label as license to skip baseline imaging altogether, rather than simply to deprioritise it [6]. The most defensible reading of the evidence taken together is that risk stratification remains useful for calibrating surveillance intensity during and after treatment -- exactly the use the validation study's own authors recommend -- while a genuinely low baseline yield across an unselected population argues against universal upfront testing on cost and burden grounds, not against baseline testing for any specific patient whose individual risk a four-category label cannot reliably resolve [3,6,7]. Put differently: the tool may be doing real work in identifying the rare very-high-risk patient who clearly needs referral, while doing comparatively little work in the much larger territory between "low" and "high," where most real patients and most real decisions actually sit.

Study limitations

This is a narrative review, not a systematic review with a pre-registered protocol, and it draws on a specific set of sources that differ in population, drug class, and endpoint definition: the O'Brien meta-analysis addresses anthracycline chemotherapy in early-stage breast cancer broadly, while the Alfehaid validation study addresses HER2-targeted therapy specifically, and the two are not directly comparable populations [3,6]. The validation study's very-high-risk category contained only 4 patients, which is too small a group to draw reliable conclusions about the tool's performance at that specific tier even though all four patients developed cardiotoxicity in that cohort [6]. This review also does not address risk stratification for other cardiotoxic drug classes -- VEGF inhibitors, immune checkpoint inhibitors, BCR-ABL tyrosine kinase inhibitors -- each of which carries a distinct cardiotoxicity profile and a separate HFA-ICOS risk tool not examined here [1]. Finally, the overscreening concern raised elsewhere in the literature -- that the breadth of guideline recommendations may already exceed what most cardio-oncology programmes can practically deliver -- is a related but distinct critique from the discrimination problem this review focuses on, and the two should not be conflated when interpreting the guidelines' overall clinical utility [5].

Conclusion

Guidelines answer the question of who needs baseline cardiac imaging before potentially cardiotoxic cancer therapy with a specific, Class I-endorsed risk stratification tool, and the case for a selective rather than universal approach is well supported by genuinely low diagnostic yield in unselected populations. But a real-world validation of that specific tool found composite cardiotoxicity rates nearly identical across its low, moderate, and high-risk categories, with discrimination barely above chance. The most defensible position, on current evidence, treats the HFA-ICOS framework as a reasonable guide to surveillance intensity and to identifying the rare very-high-risk patient who clearly needs referral, while stopping short of treating any individual patient's low-risk label as strong reassurance that baseline imaging can be safely skipped altogether.

1. Lyon AR, Lopez-Fernandez T, Couch LS, et al. "2022 ESC Guidelines on cardio-oncology". *Eur Heart J* 43(2022):4229-4361.
2. Lyon AR, Dent S, Stanway S, et al. "Baseline cardiovascular risk assessment in cancer patients scheduled to receive cardiotoxic cancer therapies: a position statement". *Eur J Heart Fail* 22(2020):1945-1960.
3. O'Brien PC, et al. "The clinical utility of baseline cardiac assessments prior to adjuvant anthracycline chemotherapy in breast cancer: a systematic review and meta-analysis". *Breast Cancer Res Treat* 174(2019):357-363.
4. Dobson R, Ghosh AK, Ky B, et al. "BSE and BCOS Guideline for Transthoracic Echocardiographic Assessment of Adult Cancer Patients Receiving Anthracyclines and/or Trastuzumab". *JACC CardioOncol* 3(2021):1-16.

5. Witteles RM, Reddy SA. "ESC cardio-oncology guidelines: a triumph -- but are we overscreening?". *JACC CardioOncol* (2022).
6. Alfehaid L, Alsuhebany N, Alamer K, Alanazi AS, Skouri H. "Clinical utility of the HFA-ICOS risk tool in real-world HER2-positive breast cancer patients receiving therapy". *Cardio-Oncology* (2026).
7. Ebrahimi S, Namburu LV, et al. "Time to personalize surveillance for cancer therapy-related cardiac dysfunction in HER2-targeted therapy: one size does not fit all". *Curr Heart Fail Rep* 23(2026):37.

Cite this article: Wenger-Baumann A, Kinsella-Byrne C, Radomska S. Cardio-Oncology at the Point of Referral: Who Needs Baseline Imaging and Who Does Not. *J Heart Cardiovasc Sci.* 2022; 3: 031-036.