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STANDARDS

Synoptic reporting of echocardiography in carcinoid heart disease (ENETS Carcinoid Heart Disease Task Force)

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Abstract

Background: This European Neuroendocrine Tumor Society (ENETS) Expert Consensus document aims to provide practical guidance and standardization for echocardiography in the screening and follow-up of carcinoid heart disease (CHD) in patients with a neuroendocrine tumour (NET) and carcinoid syndrome.

Methods: NET experts within the ENETS Carcinoid Heart Disease Task Force reviewed both general reporting guidelines and specialized scoring systems for transthoracic echocardiography (TTE) in CHD. Based on this review, a dedicated template report was designed by the multidisciplinary working group of cardiologists, oncologists, endocrinologists, gastroenterologists, surgeons and radiologists.

Results: We propose a Synoptic Reporting of Echocardiography in Carcinoid Heart Disease which represents an agreed peer reviewed proforma to capture information at the time of referral and enable a detailed outcome of CHD assessment. This

includes a systematic and detailed list of structures to evaluate data to capture at the time of reporting of TTE.

Conclusions: Adherence to these reporting guidelines aims to promote homogeneous and detailed evaluation of CHD to secure accurate assessment and allow comparison of studies performed intra- and inter-individually. These guidelines could also facilitate CHD assessment as part of prospective clinical trials to enable standardization of the findings seen in response to therapy.

KEYWORDS

carcinoid heart disease, echocardiography, neuroendocrine neoplasia, synoptic reporting

1 | INTRODUCTION

Carcinoid heart disease (CHD) is a severe complication of the carcinoid syndrome, which is the most prevalent hormonal syndrome in patients with neuroendocrine tumours (NETs), particularly those of small intestinal origin. It was first described in the 1950s as right-sided valvular disease in a series of patients with small bowel NETs and extensive abdominal metastases.[1,2] Current data estimate the prevalence of CHD in 20%–50% of patients with carcinoid syndrome,[3] which in itself is observed in approximately 20% of patients with a gastrointestinal or pulmonary NET.[4] The importance of screening and identification of CHD relies on this being a well-recognized independent negative prognostic indicator for survival from historic case series.[5,6]

CHD is characterized most frequently by tricuspid valve (TV) and pulmonary valve (PV) regurgitation and stenosis.[7] At a histological level, there is increased deposition of fibrous tissue on the cardiac valves, endocardium and rarely the intima of the major vessels, leading to the formation of plaque-like structures.[8] The affected heart valves undergo a progressive process of thickening, retraction and fixation, ultimately contributing to impaired function. The endocrine release of bioactive peptides and amines most often by liver metastases of NETs are considered major drivers to the development of CHD. Circulating serotonin (or 5-hydroxytryptamine) is considered the predominant causative factor in CHD development through stimulation of the serotonin receptor subtype 2B on endocardial fibroblasts and smooth muscle cells and release of paracrine profibrotic factors, although confirmation of this process is pending. In approximately one-third of cases, CHD can also affect the left-sided valves (aortic valve in 29%, and mitral valve in 27%), not only in patients with co-existing patent foramen ovale (PFO), but also in those with bronchial NET with a high level of serotonin production.[7]

Patients suffering from CHD can be asymptomatic, but eventually develop progressive symptoms of (exertional) dyspnoea and fatigue, together with common signs of right-sided heart failure, including elevated jugular venous pressure, hepatomegaly and peripheral oedema. Findings on auscultation of the heart depend on the valves involved but it is important to note that clinical detection of right-sided heart valve lesions based on such findings lacks sensitivity. The development of severe CHD and onset of symptoms is highly variable and can be rapid, occurring in some over a matter of months.[3] All patients with carcinoid syndrome should be screened for CHD because this has major prognostic implications evidenced by the limited 3-year survival of approximately 30% in patients with untreated CHD.[3] Following the diagnosis of CHD, initiation of medical management of symptomatic patients is generally associated with an improvement in clinical condition, whereas the impact on prognosis remains unclear. Of utmost importance, the diagnosis of CHD of any grade in individual patients should prompt discussion within an expert multidisciplinary team of the indications and timing of valve replacement relative to medical management.

1.1 | Screening and diagnosis of CHD

Screening of CHD should be considered in all patients with carcinoid syndrome and/or elevated levels of 5-HIAA,[3] especially in patients at higher risk of development of CHD, including patients with liver metastases or with uncontrolled or refractory carcinoid syndrome. Patients with primary ovarian or lung NETs or patients with retroperitoneal metastases are at high risk of CHD even in the absence of liver metastases. Furthermore, patients with fibrosis around mesenteric metastases seem to have a higher risk of developing CHD in the future.[9]

A variety of screening techniques for CHD have been explored over the years. Transthoracic echocardiography (TTE) constitutes the key modality in the evaluation of CHD and in the assessment of its disease severity. In those patients in whom TTE is technically difficult or where images are too poor quality to exclude CHD, transoesophageal echocardiography may be a useful but semi-invasive tool. Alternatives such as cardiac magnetic resonance imaging may be an option[7] and can offer advantages in accurate quantification of ventricular structure and function in response to CHD, thereby enabling a more comprehensive assessment.[10] Likewise, cardiac computed tomography (CT) can be useful for valve assessment in suspected CHD, particularly of the PV (which is difficult to assess

with TTE), and offers further advantages, including imaging of the coronary arteries and of cardiac metastases. Cardiac CT is especially useful in patients who are considered for surgical intervention.[11]

This document follows the European Neuroendocrine Tumor Society (ENETS) consensus guidelines for the standard of care for echocardiography, published in 2009.[12] Participants of the multidisciplinary CHD Task Force within the ENETS Advisory Board developed the present standardized reporting form of echocardiography for assessment and follow-up of CHD. This synoptic reporting guideline aims to homogenize practice in CHD assessment by TTE and reporting between individual operators and different institutions, a clear unmet need in NET practice.[13]

2 | METHODS

2.1 | Literature review

A systematic review was undertaken to mine the literature for echocardiography reporting in CHD. Embase and Medline databases were searched from inception until 19–05–2021 with the following search strings: ('carcinoid syndrome'/de OR ((carcinoid NEXT/1 (syndrome* OR heart OR cardiac OR flush)) OR carcinoidosis OR carcinoidoses):Ab,ti) AND (echocardiography/exp OR echography/de OR 'Doppler ultrasonography'/de OR (echocardiogra* OR echogra* OR ultraso* OR tte OR Doppler*):Ab,ti) AND ('scoring system'/de OR 'reporting and data system'/de OR 'diagnostic accuracy'/de OR 'diagnostic test accuracy study'/de OR 'disease severity'/de OR 'disease severity assessment'/de OR quantification/de OR prediction/de OR (((scoring OR reporting OR grading) NEAR/3 (system* OR assessment*)) OR (diagnostic NEAR/3 accura*) OR severit* OR quantif* OR predict* OR (echocardiogra* NEAR/3 (feature* OR spectrum* OR characteristic*))):ab,ti) NOT ('case report'/de OR case-report*:ti) AND [english]/lim NOT [conference abstract]/lim NOT ([animals]/lim NOT [humans]/lim) for Embase, (Malignant Carcinoid Syndrome/ OR ((carcinoid ADJ (syndrome* OR heart OR cardiac OR flush)) OR carcinoidosis OR carcinoidoses).ab,ti.) AND (exp Echocardiography/ OR Ultrasonography/ OR Ultrasonography, Doppler/ OR (echocardiogra* OR echogra* OR ultraso* OR tte OR Doppler*).ab,ti.) AND (Clinical Decision Rules/ OR Severity of Illness Index/ OR Forecasting/ OR (((scoring OR reporting OR grading) ADJ3 (system* OR assessment*)) OR (diagnostic ADJ3 accura*) OR severit* OR quantif* OR predict* OR (echocardiogra* ADJ3 (feature* OR spectrum* OR characteristic*))).ab,ti.) NOT (case reports/ OR case-report*.ti.) AND english.la. NOT (exp animals/ NOT humans/) for Medline.

In total, 124 records were retrieved from the two databases. After the removal of duplicates, 88 publications were left for assessment of eligibility. After screening title and abstract for clinical reports on echocardiography reporting in CHD, 17 publications contained relevant information for the current consensus guideline. After evaluation of the full-text articles, six publications with original CHD scoring systems remained.

2.2 | Drafting of the standardized reporting template

The validity and clinical applicability of the available echocardiography scoring systems was discussed among a dedicated working group within the CHD Task Force of the ENETS Advisory Board. A template for a standardized report was drafted based on the expert consensus document on adult TTE reporting from the European Association of Cardiovascular Imaging[14] and on the Royal Free Carcinoid Heart Disease Score.[15] The initial draft was discussed among the expert working group, comprised of cardiologists, oncologists, endocrinologists, gastroenterologists, surgeons and radiologists. Important aspects for the standardized echocardiography report included its use in both neuroendocrine neoplasm and non-referral centres, for screening as well as follow-up of documented CHD and following valve replacement. A majority consensus was reached for each data element by iterative discussions of the synoptic reporting draft. The pre-final template was circulated for feedback to the complete CHD Task Force and adopted according to provided suggestions.

3 | RESULTS

The Synoptic Carcinoid Echocardiography Report is available in Table 1.

3.1 | Transthoracic echocardiography: basic principles for CHD assessment

When performing TTE, evaluation of the thickening, mobility and retraction of leaflets/cusps of valves is of crucial importance. CHD is a heterogeneous disease, with a wide spectrum of echocardiographic findings. Findings may vary from mild, isolated thickening of a single valve leaflet/cusp with no significant reduction in leaflet/cusp mobility, to advanced thickening, retraction and immobility of multiple leaflets/cusps with associated severe valve disease.[7] For assessment of the leaflet thickness, the most affected leaflet/cusp should be assessed in zoomed views in a frame without valve motion, with leaflets/cusps whenever possible perpendicular to the echocardiographic beam, taking advantage of the axial resolution. Measurements should be taken three times and averaged.[16,17]

3.2 | Tricuspid valve assessment

The most frequently affected valve in CHD is the TV with involvement in 90% of cases.[7] It is the largest and most apically positioned valve and consists of the fibrous annulus with the three leaflets (anterior, posterior and septal), the papillary muscles and chordae.[18–20] The three TV leaflets vary in both circumferential (annular) and radial size. The anterior leaflet is the longest radial

TABLE 1 Synoptic Carcinoid Echocardiography Report

Clinical details (to be filled in at time of TTE by the requesting clinical team)		
Patient details	Date of birth: __/__/_____ Patient ID: _____	
Gender	Female Male	
Indication for TTE	Screening (suspected CHD) Follow-up (known CHD)	
Referring physician	_____	
Assessment at time of TTE		
Date of TTE	Date: __/__/_____	
Time of TTE	__:__ am/pm	
Study Location	_____	
Performed by	_____	
Previous cardiac surgery	Yes which _____ No	
If valve surgery in the past	Biological valve Metallic valve Size of valve replacement _____ Type of valve replacement _____	
Blood pressure	___/____ mmHg	
Heart rate	___ bpm	
Heart rhythm	Sinus rhythm Other which _____	
Height	_____ cm	
Weight	_____ kg	
BSA	_____ m^2	
Technique		
Quality of cardiac images	Good Fair Poor	
Right-sided valvular assessment		
Tricuspid valve		
Valve apparatus description:	_____	
Regurgitation, vena contracta width with Nyquist limit 50–70 cm/sec:	___mm Score	CHD score
	Normal	0
	< 3 mm: Mild	1
	3–6 mm: Moderate	2
	> 6 mm: Severe	3
Stenosis, mean pressure gradient:	___ mmHg	
	Normal	0
	< 5 mmHg: Mild	1
	5–8 mmHg: Moderate	2
	>8 mmHg: Severe	3
Leaflet description (describe the most severely affected leaflet):		
Leaflet thickening (mm)	Normal	0
	≥ 3 to < 4: Mild	1
	≥ 4 to < 5: Moderate	2
	≥ 5: Severe	3

(Continues)

TABLE 1 (Continued)

Leaflet excursion	Normal	0
	> 50 to ≤ 75% of normal:Mild	1
	> 25 to ≤ 50% of normal:Moderate	2
	≤ 25% of normal of fixed:Severe	3
Leaflet retraction	Normal	0
	Mild	1
	Moderate	2
	Severe	3
Pulmonary valve		
Valve apparatus description:	_____	
Regurgitation, vena contracta width with Nyquist limit 50–70 cm/sec	___ mm ___ ms	
Regurgitation, pressure half time of PR jet: Regurgitation, PR index[#]	___	CHD Score
	Normal	0
	< 3 mm: Mild	1
	3–6 mm: Moderate	2
	> 7 mm: Severe	3
Stenosis, V_{max}	___ m/s	
	Normal	0
	<3 m/s: Mild	1
	3–4 m/s: Moderate	2
	> 4 m/s: Severe	3
Leaflet description (describe the most severely affected cusp):		
Cusp thickening (mm)	Normal	0
	≥ 3 to < 4: Mild	1
	≥ 4 to < 5: Moderate	2
	≥ 5: Severe	3
Cusp excursion	Normal	0
	> 50 to ≤ 75% of normal: Mild	1
	> 25 to ≤ 50% of normal: Moderate	2
	≤ 25% of normal of fixed:Severe	3
Cusp retraction	Normal	0
	Mild	1
	Moderate	2
	Severe	3
Right ventricular/atrial assessment		
Findings	_____	
Right atrial area	___ cm^2	
Right ventricular basal diameter (25–41 mm) RV mid diameter (normal 19–35 mm)	___ mm ___ mm	CHD score
	RV < 2/3 of LV size: Normal	0
	RV = LV size Mild dilatation	1
	Larger than LV size Moderate dilatation	2
	Much larger than LV Severe dilatation	3
Right ventricular function		
TAPSE (normal > 17 mm)	_____	

(Continues)

TABLE 1 (Continued)

RV area change (normal > 35%)	_____%	
Visual assessment	_____	CHD score
Integrated RV assessment	Normal	0
	Mild impairment	1
	Moderate impairment	2
	Severe impairment	3
Left-sided valvular assessment		
Mitral valve		
Valve apparatus description:	_____	
Regurgitation, vena contracta width	___ mm	CHD score
	Normal	0
	< 3 mm: Mild	1
	3–6 mm: Moderate	2
	≥ 7 mm: Severe	3
Stenosis, mean pressure gradient:	___ mmHg	
Stenosis, mitral valve area:	___ cm	
	Normal	0
	< 5 mmHg or > 1.5cm:Mild	1
	6–10 mmHg or 1–1.5 cm: Moderate	2
	> 10 mmHg or < 1.0 cm: Severe	3
Leaflet description (describe the most severely affected leaflet):		
Leaflet thickening (mm)	Normal	0
	≥ 3 to < 4: Mild	1
	≥ 4 to < 5: Moderate	2
	≥ 5: Severe	3
Leaflet excursion	Normal	0
	> 50 to ≤ 75% of normal: Mild	1
	> 25 to ≤ 50% of normal: Moderate	2
	≤ 25% of normal of fixed: Severe	3
Leaflet retraction	Normal	0
	Mild	1
	Moderate	2
	Severe	3
Aortic valve		
Valve apparatus description:	_____	
Regurgitation, vena contracta width	___ mm	
	Normal	0
	< 3 mm: Mild	1
	3–6 mm: Moderate	2
	> 6 mm: Severe	3
Stenosis, V_{max}	___ m/s	
Stenosis, mean pressure gradient	___ mmHg	
	Normal	0
	< 3 m/s or < 20 mmHg: Mild	1
	3–4 m/s or 20–39 mmHg:Moderate	2
	> 4 m/s or > 40 mmHg:Severe	3

(Continues)

TABLE 1 (Continued)

Cusp description (describe the most severely affected cusp):		
Cusp thickening (mm)	Normal	0
	≥ 3 to < 4: Mild	1
	≥ 4 to < 5: Moderate	2
	≥ 5: Severe	3
Cusp excursion	Normal	0
	> 50 to ≤ 75% of normal: Mild	1
	> 25 to ≤ 50% of normal: Moderate	2
	≤ 25% of normal of fixed: Severe	3
Cusp retraction	Normal	0
	Mild	1
	Moderate	2
	Severe	3
Carcinoid heart disease score		
Score tricuspid valve	___	
Score pulmonary valve	___	
Score mitral valve	___	
Score aortic valve	___	
Score right ventricle	___	
Total carcinoid heart disease score	___	
Left ventricular/atrial assessment		
Findings	_____	
Left atrial Volume	___ml	
LV size		
EDD	___mm	
ESD	___mm	
EDV	___ml	
ESV	___ml	
LVEF	____ %	
Structural abnormalities	_____	
Patent foramen ovale	Present	
	Present	
	Not assessed	
Other relevant findings	Free text:	
Conclusions	Free text:	

Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; bpm, beats per minute; BSA, body surface area; CHD, carcinoid heart disease; cm, centimetre; EDD, end diastolic diameter; EDV, end diastolic volume; ESD, end systolic diameter; ESV, end systolic volume; ID, identification number; kg, kilogram; LVEF, left ventricular ejection fraction; m, metres; mmHg, millimetres of mercury; MR, mitral regurgitation; MS, mitral stenosis; PHT, pressure half-time; PR, pulmonary regurgitation; PS, pulmonary stenosis; TAPSE, Tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; TS, tricuspid stenosis; TTE, transthoracic echocardiography.

#PR index: Duration of the PR signal divided by the total duration of diastole

leaflet with the largest area and the greatest motion. The septal leaflet is the shortest in the radial direction and the least mobile. The posterior leaflet is the shortest circumferentially.[21] The complex anatomy of TV makes it difficult to visualize all three leaflets in one 2D view; hence, multiple views, extensively described in the guidelines of the American and British Societies of Echocardiography,[22–24] should be utilized. Despite this, it is not always possible on 2D imaging to identify individual leaflets with a sufficient degree of accuracy. The four-chamber view (A4C), parasternal long axis (PLAX) view of right ventricular inflow and parasternal short axis (PSAX) views are mandatory.[21] Subcostal views can also be useful but it should be noted that, in patients with CHD with large liver metastases, subcostal views are frequently unobtainable. Inflow velocities are affected by respiration; hence,

all measurements taken must be averaged throughout the respiratory cycle or recorded at end-expiratory apnoea. In patients with atrial fibrillation, measurements from a minimum of five cardiac cycles should be averaged. Whenever possible, it is best to assess the severity of the disease (especially severity of tricuspid stenosis) at heart rate less than 100 bpm and preferably between 70 and 80 bpm.

3.3 | Pulmonary valve assessment

The PV is the second most affected valve in CHD with a prevalence of 69%.[7] The PV consists of three cusps and is supported by the pulmonary root, which is part of the right ventricular outflow tract (RVOT). There are three pulmonary sinuses of Valsalva, formed by the semilunar attachments of the valve leaflets proximally and the sinotubular junction distally.[25] The pulmonary valve sinuses are labelled in relation to the aortic sinuses; the three sinuses can be anterior, right and left posterior sinuses.[26] The infundibulum places the pulmonary valve above the ventricular septum, in a superior position that offers a unique advantage for resection of the pulmonary valve leaflets during surgery. The PV is imaged by TTE from the PLAX view of RVOT and pulmonary artery, the PSAX view of bifurcation of pulmonary artery and the PSAX view of basal right ventricle. The subcostal short axis view of basal right ventricle can be explored as well but, as mentioned above, subcostal views for patients with CHD are rarely obtainable. Echocardiographic visualization of the PV is more difficult than for other valves, and usually only one or two cusps will be visualized simultaneously.[22] Overall, PV involvement may be underappreciated with echocardiography and careful, comprehensive investigations using 2D, 3D, colour-flow and spectral Doppler imaging are needed to provide a thorough assessment.

3.4 | Right atrium and ventricle assessment

The assessment of right-sided structures was the topic of specific guidelines of ASE endorsed by the European and Canadian Societies.[22] In accordance with current guidelines, assessment of right atrial and right ventricular (RV) structure and function should be performed from a modified A4C view, in which the maximum basal dimension of the Right Ventricle is seen.[22] The Right Ventricle is usually smaller than the Left Ventricle in a standard A4C view and, if the apex of the heart is shared or occupied by the Right Ventricle, this is an indication of volume overloading and dilatation. In advanced CHD with severe TV and/or PV regurgitation, the RV ventricle may measure within the normal reference limits but appears larger than the small, underfilled left ventricle. The basal RV diameter is defined as the maximal short-axis dimension in the basal one-third of the right ventricle seen on the four-chamber view. In the normal right ventricle, the maximal short-axis dimension is located in the basal one-third of the ventricular cavity.

3.5 | Assessment of left-sided heart and foramen ovale

Because left-sided CHD can be present in a minority of patients and left-sided valvular or ventricular disorders are more often the result of degenerative, structural or ischaemic diseases, a dedicated description of the mitral and aortic valves as well as left ventricular and atrial size and function should be included in CHD echocardiography reporting.

Agitated saline contrast echocardiography should be performed to detect PFO in patients with confirmed CHD.[27] To this end, a 20- to 22-gauge Abbocath is placed into the antecubital vein and connected to a three-way tap. Two Luer lock 10-mL syringes are attached to the three-way tap. One of the syringes is filled with 8.5 mL of saline, 1.0 mL of blood is withdrawn from the vein into the syringe and 0.5 mL of air is added to the 'mixture'. Saline, blood and 0.5 mL of air are mixed between 2 Luer lock syringes attached to the three-way tap on the arm of the patient. Then a 3–5-mL bolus of the agitated mixture is injected as a bolus into the vein under ultrasound control and with continuous recording of images. The injection should be repeated under cough and Valsalva manoeuvre (release phase). A PFO is considered present when there is a transfer of microbubbles from the right atrium to the left atrium within three to five cardiac cycles. The size shunt can be defined as small (< 5 bubbles), moderate (6–25 bubbles), or severe (> 25 bubbles). Assessment of PFO is of particular importance in all patients being considered for surgery because any PFO should be closed at operation to prevent later recurrence of CHD in the left-sided valves. Performance of agitated saline testing should follow current guideline recommendations.[28]

Myocardial metastases have been reported in 4% of neuroendocrine neoplasm patients with echocardiography and are likely more often visualized with contemporary ^{68}Ga-labelled somatostatin receptor-targeted positron emission tomography imaging,[29] as well as cardiac CT or magnetic resonance imaging because the sensitivity to identify them with TTE is low.

3.6 | Validated CHD scoring systems

Following our literature review, six different scoring systems for the presence of CHD were identified,[15,30–34] which are summarized in Table 2. The feasibility and diagnostic capability of all available scoring systems were evaluated in a single prospective trial of 100 NET patients with liver metastases and/or carcinoid syndrome.[34] In this study, 21% of patients were found to have CHD on echocardiography and all had New York Heart Association Class I–II. Overall, there were no major differences between the different scoring systems in feasibility, sensitivity/specificity or correlation with biochemical markers of CHD or carcinoid syndrome, although the Royal Free Hospital CHD Score had the best correlation with N-terminal pro B-type natriuretic peptide and plasma 5-hydroxyindoleacetic acid combined with area under the

TABLE 2 Summary of Carcinoid Heart Disease Scoring systems

	Denney et al. (1998)[30]	Westberg et al. (2001)[33]	Moller et al. (2003)[32]	Bhattacharyya et al. (2008)[35]	Mansencal et al. (2010)[31]	Dobson et al. (2014)[34]
Patients screened/ with CHD (%)	23/13 (57%)	52/40 (77%)	71/50 (70%)	200/39 (20%)	80/42 (53%)	100/21 (21%)
Study design	Prospective	Retrospective	Retrospective	Prospective	Prospective	Prospective
Items scored						
Thickening	TV	TV	TV, PV	TV, PV, MV, AV	TV, PV, MV, AV	TV, PV
Mobility	TV		TV, PV	TV, PV, MV, AV	TV, PV, MV, AV	TV, PV
Retraction		TV	TV, PV	TV, PV, MV, AV		
Stenosis	PV			TV, PV, MV, AV	TV, PV	TV, PV
Regurgitation	TV, PV	TV	TV, PV	TV, PV, MV, AV	TV, PV, MV, AV	TV, PV
Right ventricle			Size, function, aberrant flow	Size, function	Size	Size, function
Right atrium						Size
Maximum score	14	8	20	66	30	33

Note: Carcinoid heart disease (CHD) scoring systems for transthoracic echocardiography were collected from literature following a systematic review. The different studies used to design the scoring systems are listed in the columns.

Abbreviations: AV, aortic valve; MV, mitral valve; PVV, pulmonary valve; TV, tricuspid valve.

curve for a diagnosis of CHD of 0.988.[34] Given our intention of a standardized report for purposes of both screening and long-term follow-up and functionality for deciding on the indication for valvular surgery, the working group based this synopsis on the Royal Free Hospital CHD score, comprising most comprehensive scoring system and incorporating all structures relevant to the CHD process. This 22-item score was developed within a prospective trial in 200 NET patients, 20% of which had a diagnosis of CHD, and had an overall excellent agreement between expert echocardiographers, with a κ value of 0.89.[15] Following an integrated approach of visual assessment of structure and function, as well as of semi-quantitative and quantitative parameters, the individual items of valvular and right ventricular abnormalities within the CHD score should be classified into three grades. Recommendations for calculation of CHD score items are provided in Table 1. It is important to emphasize that the purpose of the CHD score is to provide a baseline assessment and identify progression/worsening of valve disease. It does not define cut-offs for different grades of valve disease but instead identifies worsening of valve disease. Progression of CHD can be defined if the CHD score is increased by 25% from previous examinations, whereas new-onset CHD can be diagnosed if newly detected features of CHD were not present on previous echocardiograms.

4 | DISCUSSION

Accurate assessment of CHD is crucial for patients with advanced NETs as a result of its impact on morbidity and mortality. TTE is the current gold standard for assessment of CHD. Its role as a diagnostic tool is usually preceded by screening biomarker testing to identify patients at higher risk of CHD for whom echocardiography is indicated. However, performance and reporting of TTE in patients with suspected CHD varies between institutions.[13] The present Synoptic Reporting of Echocardiography in Carcinoid Heart Disease aims to provide a guide for homogeneous assessment of CHD at time of TTE performance. The use of synoptic over narrative reporting can lead to several improvements in the screening and surveillance of CHD, including unity, consistency, comprehensiveness and quantification.

The proposed Synoptic Reporting of Echocardiography includes details on the information required at the time of TTE request to provide a holistic clinical overview of the patient's status and rationale for testing, as well as the specific details on structures that must be evaluated during the TTE.

The clinical fields to be filled in at time of TTE being requested by the clinical team are focused on providing detailed information on the rationale for such investigation being performed, including the presence or absence of CHD symptoms, or values on biomarkers at the time of referral. In addition, data on the indication for TTE is further specified, with clear discrepancy between screening and follow-up after diagnosis of CHD. This information aims to support further CHD assessment by providing a well-defined clinical history of each individual patient.

The proposed items of information to be collected at the time of TTE performance aim to provide a systematic assessment of CHD with evaluation of all relevant structures. This detailed evaluation aims to facilitate a thorough assessment of CHD, attempting to reduce the chances of missing incipient indicators of CHD that may be otherwise under-reported. By doing so, early identification of CHD (progression) and selection of patients for valve replacement may be achieved.

Current CHD assessment and reporting varies significantly between institutions. This is one of the main reasons why the incidence and progression of CHD varies between studies. On top of this, the lack of standardized TTE reporting is also one of the main challenges for prospective studies in this setting, for which a central review of all TTE examinations may be required to overcome such a problem. The utilization of our synoptic report could facilitate homogeneous assessment of CHD between institutions, which would allow inter-institutional comparisons of CHD prevalence, severity and outcome data. In addition, it could also facilitate the delivery of prospective studies in which CHD may be one of the clinical endpoints.

In summary, our proposed Synoptic Reporting of Echocardiography in Carcinoid Heart Disease aims to provide an agreed peer-reviewed proforma to capture information at the time of referral and enable a detailed outcome of CHD assessment to provide a detailed holistic assessment of a relevant complication for patients with advanced NETs. Its use aims to enhance systematic assessment during the screening and surveillance of all relevant structures and also facilitate inter-institutional comparison of outcomes.

This article is part of a special issue on standised (synoptic) reporting of neuroendocrine tumours (see editorial[36] and articles[37-40]).

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CONFLICT OF INTERESTS

Dr Johannes Hofland reports speaker honoraria from Ipsen and advisory honoraria from Ipsen and Novartis. Dr Angela Lamarca reports travel and educational support from Ipsen, Pfizer, Bayer, AAA, SirtEx, Novartis, Mylan and Delcath; speaker honoraria from Merck, Pfizer, Ipsen, Incyte, AAA and QED; advisory honoraria from EISAI, Nutricia Ipsen, QED and Roche; and is a member of the Knowledge Network and NETConnect Initiatives funded by Ipsen. Dr Simona Grozinsky-Glasberg reports speaker and advisory board honoraria from Ipsen and Triple A and has received research grant support from Ipsen and Novartis. Dr Christos Toumpanakis reports speaker and advisory board honoraria from Novartis, IPSEN, AAA and Lexicon and has received education grants for the NET Unit from Novartis, IPSEN, AAA and Lexicon. The other authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

Johannes Hofland: Data curation; Formal analysis; Methodology; Writing – original draft. **Angela Lamarca:** Data curation; Methodology; Validation; Writing – original draft. **Rick Steeds:** Conceptualization; Data curation; Methodology; Supervision; Validation; Writing – original draft. **C. Toumpanakis:** Conceptualization; Data curation; Methodology; Supervision; Writing – review & editing. **Rajaventhan Srirajaskanthan:** Methodology; Validation; Writing – review & editing. **Rachel Riechelmann:** Methodology; Writing – review & editing. **Francesco Panzuto:** Methodology; Writing – review & editing. **A Frilling:** Methodology; Writing – review & editing. **Timm Denecke:** Methodology; Writing – review & editing. **Emanuel Christ:** Methodology; Writing – review & editing. **Simona Grozinsky-Glasberg:** Conceptualization; Investigation; Methodology; Supervision; Writing – review & editing. **Joseph Davar:** Conceptualization; Investigation; Methodology; Supervision; Validation; Writing – original draft; Writing – review & editing.

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DATA AVAILABILITY

This guideline does not have original data and therefore has no data storage/availability.

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