DZHK-SOP-C-02

Anamnesis/Clinical Diagnoses

Version: V2.0 Valid as of: 23.03.2023

Replaces version: V1.0 dated: 01.09.2014

Modification notice: Ethnicity and skin color not applicable

NEW: Vital status recording (end of study)

Diabetes mellitus (specification of threshold values)

Dyslipidemia (specification of limit values)

Degree of renal dysfunction (grade classification)

Laboratory diagnostics

This SOP is a translation from the original German SOP and valid without signatures.

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*Adapted from the SOPs of the Competence Network Heart Failure

The text elements highlighted in gray in this SOP are mandatory (= basic data set). The text elements that are not highlighted must be adhered to if possible.

CONTENTS

1 INTRODUCTION

1.1 LIST OF ABBREVIATIONS

Abbreviation	Plain text
ASD	atrial septal defect
COPD	chronic obstructive pulmonary disease
CRT	cardiac resynchronization therapy
CT	computed tomography
eCRF	electronic Case Report Form
eGRF	estimated Glomerular Filtration Rate
ECG	electrocardiogram
FFR	fractional flow reserve
GFR	glomerular filtration rate
HDL cholesterol	high-density lipoprotein cholesterol
IABP	intra-aortic balloon pump
ICD	implantable cardio-verter defibrillator
IVUS	intra-vascular ultrasound
LDL cholesterol	low-density lipoprotein cholesterol
MDRD formula	Modification of Diet in Renal Disease formula
MRT/MRI	magnetic resonance tomography/magnetic resonance imaging
NIH Stroke Scale	National Institutes of Health Stroke Scale
NYHA	New York Heart Association
OCT	optical coherence tomography
PAOD	peripheral arterial occlusive disease
PTCA	percutaneous transluminal coronary angioplasty
QRS	QRS complex in ECG (action potential duration)
RV	right ventricle
S_{Cr}	serum creatinine
TIA	transient ischemic attack
VSD	ventricular septal defect
CVP	central venous pressure
s/p	status post

WG	working group

1.2 OBJECTIVE

Uniform definitions are proposed in the context of this SOP when a corresponding risk factor/clinical diagnosis is considered to be present.

1.3 TARGET GROUP

This SOP is intended for individuals who make entries into the basic data module ‚Anamnesis'. These may be e.g. physicians or study assistants.

1.3.1 Inclusion Criteria

Included are all patients who meet the respective inclusion/exclusion criteria of the respective study.

1.3.2 Exclusion Criteria

None. If information cannot be collected in full, it should be collected to the greatest extent possible.

1.4 APPLICATION AND TASKS

The purpose of the anamnesis/clinical diagnoses is to accurately record known cardiovascular risk factors. The anamnesis is a core element of medical diagnostics. The findings obtained allow a detailed estimation of a person's cardiovascular risk.

Collection of the anamnesis/clinical diagnoses is an integral part of all observational and clinical studies of the DZHK. The exact implementation of the DZHK basic data set is described in the item catalog. There, as well as in all eCRFs, all mandatory basic items are marked with **.

1.5 TERMS AND DEFINITIONS

Date of examination

- is defined as the date on which the examination takes place**.**

Sex and date of birth

- are defined as the data which appear on the person's identity card.

Height and weight

- Height: Measured standing, without socks and without headgear. Weight: Measured in usual street clothes, without jacket and without shoes. Preferably, measurements should be taken; only if this is not possible (e.g. bedridden persons) should the data be estimated or based on anamnestic information from the participant.

Ethnicity: Caucasian

- Ethnic origin is defined by a person's ancestry with respect to a particular population group. This can be determined biologically and or geographically by a certain settlement affiliation. The classification Caucasian means here light-skinned people of European origin.

Familial predisposition of myocardial infarction or stroke

- is defined as a medically diagnosed myocardial infarction or stroke in one or both biological parents, biological siblings (including half-siblings) or biological children, provided the female relative was under age 65, or the male relative under age 60 (at the time of the myocardial infarction/stroke).

Diabetes mellitus

- is defined as diabetes which has been diagnosed and/or treated by a physician.
    - American Diabetes Association criteria include:
        - hemoglobin A1c ≥ 6.5 % (48 mmol/mol Hb) or a fasting blood glucose level of ≥ 126 mg/dl (7.0 mmol/l) or a 2-hour blood glucose level of ≥ 200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test.

Arterial hypertension

- is defined as a current or previous medical diagnosis of arterial hypertension, treated with diet, exercise, and/or medication. Systolic blood pressure values ≥ 140 mmHg and/or diastolic blood pressure values ≥ 90mmHg measured by a physician on at least two separate days after a 5-minute resting phase qualify for a diagnosis of arterial hypertension.

Dyslipidemia

- is defined as a current or previous diagnosis of dyslipidemia which was diagnosed and/or is being treated by a physician.
- one or more of the following criteria:
    - total cholesterol ≥ 190 mg/dl (5mmol/l),
    - LDL cholesterol ≥ 115 mg/dl (3mmol/l),
    - HDL cholesterol < 40 mg/dl (1mmol/l) (men) and < 45 mg/dl (1,2 mmol/l) (women).

Smoker

- is defined as current or previous use of cigarettes, cigars, pipes, hookah, e-cigarette or smokeless tobacco.
  "Yes" for daily or occasional smoking (≥ 1x/month) even with abstinence of less than 6 months;
  "Ex-smoker" if abstinent for more than 6 months; ex-smoker since …;
  "No" for "never smoked".

Pack years

- the product of the number of years of cigarette smoking multiplied by the average number of packs smoked per day.
  Example: A patient who has smoked 2 packs of cigarettes per day for 20 years has 40 pack years.

Drinks per week

- the number of alcoholic drinks consumed per week. One drink is defined as e.g. 0.25 l of beer, 0.1 l of wine or 0.02 l of spirits. Example: A person who drinks 0.5 l beer twice a week on average has 4 drinks per week.

Medically diagnosed alcoholism

- is defined as a current or previous physician's diagnosis of alcoholism.

Renal failure

- any participating individual who has a renal function impairment as diagnosed by a physician.

Degree of renal dysfunction

- if known, the degree of renal dysfunction should be quantified using the estimated glomerular filtration rate (eGFR). There are different methods for estimation, but if available, the MDRD formula should be used. It is:

$$eGFR(ml/min) =$$
$$= 186 \times (S_{Cr})^{-1,154} \times (Alter)^{-0,203} \times (0,742\text{falls weiblich}) \times (1,210\text{falls schwarze Hautfarbe})$$
$$= exp(5,228 - 1,154 \times ln(S_{Cr}) - 0,203 \times ln(Alter) - (0,299\text{falls weiblich}) + (0,192\text{falls schwarze Hautfarbe}))$$

  - eGFR: estimated glomerular filtration rate
  - S_{Cr}: serum creatinine in mg/dl
  - age: age in years

Based on the results, the following grade classification is made:

1 – eGFR 90 ml/min or higher

2 - eGFR 60-89 ml/min

3 - eGFR 30-59 ml/min

4 - eGFR 15-29 ml/min

5 - eGFR < 15 ml/min or current dialysis requirement

Unknown

Not raised

Current dialysis dependency

- is defined as current regular, at least weekly, renal replacement therapy (including hemodialysis and peritoneal dialysis) within the last 30 days.

Coronary heart disease

- is defined as a current or previous medical diagnosis with one or more of the following criteria:
  - coronary artery stenosis of ≥ 50 % (diagnosed by cardiac catheterization or another direct coronary artery imaging method),
  - previous coronary artery bypass operation,
  - previous percutaneous coronary intervention,
  - arteriosclerosis-induced myocardial infarction.

Condition post myocardial infarction

- is a physician's diagnosis of the disease. Rationale: Acute myocardial infarction is defined as evidence of myocardial necrosis in a clinical setting consistent with myocardial infarction.

  One or more of the following criteria must apply:

  - Evidence of an increase or decrease of a cardiac biomarker (preferably troponin) with at least one value above the 99 % percentile of the upper reference limit and, additionally, at least one of the following factors:
    - Ischemic symptoms,
    - ECG changes indicative of new ischemia, e.g. ST segment changes or a new left bundle branch block, development of pathological Q waves in the ECG,
    - imaging studies show a loss of viable myocardial tissue or new regional kinetic abnormalities,
    - angiographic evidence of stenosis/vascular occlusion.

Cardiomyopathy

- is defined as a physician's diagnosis of a primary heart muscle disease. If the response to this question is "yes", further data is collected in the "Cardiomyopathy Diagnostics" form.

Heart failure

- is defined as a current or previous physician-documented diagnosis of heart failure, based on the following symptoms: shortness of breath with mild exertion, recurrent shortness of breath when sitting, fluid overload or pulmonary rales, jugular venous congestion, pulmonary edema on physical examination or pulmonary edema on chest x-rays. Documentation of reduced left

ventricular function alone in the absence of clinical signs of heart failure does not meet the criteria for heart failure.

Status post decompensation is defined as any previous admission to a hospital with symptoms of heart failure (see above).

Initial diagnosis of heart failure is defined as the time point when heart failure was diagnosed for the first time by a physician. Hence, it does not refer to the time point of first onset of symptoms, which is often much earlier.

NYHA class: Classification of the patient's symptoms based on the New York Heart Association classification of heart failure:

- NYHA I: No complaints
- NYHA II: Complaints with greater exertion
- NYHA III: Complaints during light exertion
- NYHA IV: Complaints at rest

Atrial fibrillation/flutter

- is defined as a current or previous physician's diagnosis of atrial fibrillation or atrial flutter. It is determined as persisting for at least 30 seconds or evidence on surface ECG.

Current or previous medical diagnosis of heart valve disease

- is defined as heart valve disease (insufficiency or stenosis), which has been diagnosed and/or treated by a physician. A more precise differentiation and severity classification of valvular heart disease will be made on the echocardiography form if an echocardiogram is documented as part of the study.

Medically diagnosed endocarditis

- If at any time, currently or in their previous medical history, a person has been diagnosed with endocarditis (heart valve inflammation), it will be documented here.

Physician diagnosed congenital heart defect

- If a patient has a known congenital heart defect, this is coded here. Congenital heart defects include shunt vitia defects (e.g. ASD, VSD), congenital valvular heart diseases (e.g. pulmonary stenosis) and cardiomyopathies diagnosed in the first five years of life. Patent foramen ovale does not belong to the class of congenital heart defects.

Interventional coronary revascularization

- is defined as an intervention performed transcutaneously on a coronary vessel, e.g. PTCA, stent implantation, rotablation et cetera. Purely diagnostic measures (intravascular ultrasound (IVUS), optical coherence tomography (OCT)) as well as functional measurements (e.g. fractional flow reserve (FFR) measurements) are not interventional coronary revascularization procedures. Where applicable, the date of the last intervention should be entered.

Peripheral revascularization

- is defined as an intervention performed transcutaneously on a peripheral vessel (excluding coronary vessels or bypass grafts), e.g., PTA, stent implantation, rotablation, etc. If applicable, enter the date of the last intervention. Ablation procedures (e.g., renal denervation) are not peripheral revascularization. Where applicable, the date of the last intervention should be entered.

Coronary bypass operation

- is defined as surgical myocardial revascularization using bypass graft (e.g. from the mammary artery or using arterial/venous grafts). Where applicable, the date of the most recent surgery should be entered.

Other vascular operation

- is defined as surgery of any kind on non-coronary vessels. Where applicable, the date of the most recent surgery should be entered.

Heart valve operation

- is defined as a minimally invasive percutaneous (catheter-based) or open surgical procedure on a heart valve. This includes the surgical reconstruction/replacement of heart valves, valvuloplasty procedures as well as interventional treatment of heart valve diseases (e.g. blasting, implantation of prostheses, repair of heart valves). Where applicable, the date of the most recent surgery should be entered. The most recent event is to be coded according to type, whereby any transapical aortic valve replacements are to be coded as "catheter-based". In addition, details of the surgical procedure should be given.

Implantable pacemaker or defibrillator

- is defined as condition after implantation of a pacemaker or intracardiac defibrillator (ICD). Where applicable, the date of the most recent operation (implantation/exchange) should be entered. The number of probes currently connected to the pacemaker device is also coded. A device with only one probe is to be coded as a 1-chamber pacemaker, a device with atrial and ventricular probes as a 2-chamber pacemaker. Devices for cardiac resynchronization therapy, with two ventricular probes, are to be coded as a biventricular pacemaker (CRT).

Other devices

- are defined as other implantable devices for cardiac/vascular support. This includes devices for cardiac contractility management, for neuromodulation (e.g. vagus nerve stimulator, baroreceptor stimulator), intra-aortic balloon pumps and left ventricular cardiac assist devices.

Status post myocardial biopsy

- is defined as status post bioptic removal of tissue from the myocardium (e.g. during a right/left catheter examination or surgery). Where applicable, the sampling site as well as the date of the most recent myocardial biopsy should be coded.

OTHER DIAGNOSES

PAOD

- is defined as a current or previous diagnosis by a physician of peripheral arterial occlusive disease (pelvic-leg vessels or upper extremity from the subclavian artery to distal). Renal, coronary, cerebral and mesenteric vessels and aneurysms are excluded. Possible symptoms are:
  - intermittent claudication,
  - pain at rest,
  - amputation due to severe arterial vascular insufficiency,
  - vascular reconstruction, bypass surgery or percutaneous revascularization,
  - a positive non-invasive test (e.g. ankle-brachial index of ≤ 0.9, pathological $TCPO_2$ measurement, evidence of 50 % or greater stenosis of a peripheral artery by Doppler/duplex sonography, CT, MRT, or angiography).

Classification of the degree of severity is done according to the Fontaine classification:

Classification according to Fontaine

Stage	**Clinical Picture**
I.	Asymptomatic PAOD
II.	Intermittent claudication - with walking distances > 200 metres (Stage IIa) - with walking distances < 200 metres (Stage IIb)
III.	Pain at rest
IV.	Necrosis, gangrene

Acute ischemic occlusion refers to a currently (in the last 30 days) occurring proven acute ischemic occlusion of a peripheral arterial vessel.

Stroke/TIA

is defined as a current or previous diagnosis by a physician of:

- Ischaemic stroke: Infarction of tissue of the central nervous system, either symptomatic or silent (asymptomatic).
- Transient ischaemic attack (TIA): A transient episode of neurological dysfunction caused by focal cerebral, spinal cord or retinal ischaemia without acute infarction, which resolves completely within 24 hours. This definition is not met by chronic (non-vascular) neurological diseases or other acute neurological diseases such as metabolic or ischaemic encephalopathy resulting from general hypoxia (e.g. respiratory failure, post cardiovascular arrest).
- Hemorrhagic stroke: Neurological dysfunction caused by intra-cranial bleeding.
- Stroke where there is uncertainty as to whether the cause was hemorrhagic or ischaemic.

Severity of the stroke: A stroke is considered “minor“ if neurological symptoms can be completely reversed within 30 days or the change in the NIH Stroke Scale (see Appendix 7.3 NIH Stroke Scale) is less than 3 points compared to the NIH Stroke Scale before the stroke. A stroke is considered “major” if neurological deficits are still detectable 30 days after the event or the NIH Stroke Scale is at least 3 points higher than prior to the stroke.

Consequences of the stroke: A stroke is considered “disabling” if the modified Ranking Scale score is greater than 2 90 days after the stroke. If the modified Rankin Scale score is 2 points or less 90 days after the stroke, the stroke is considered “non-disabling”.

The modified Rankin Scale of 0 to 6 describes the range from complete health to death.

- 0 - No symptoms.
- 1 - No significant impairment. Can perform daily activities despite some symptoms.
- 2 - Slight impairment. Is able to care for him or herself without assistance, but is limited in daily activities.
- 3 - Moderate impairment. Requires assistance in daily life, but is able to walk without assistance.
- 4 - More severe impairment. Requires assistance with personal hygiene; is not able to walk without assistance.
- 5 - Severe impairment. Bedridden, incontinent, requires constant nursing assistance.
- 6 – Death caused by apoplexy.

Chronic lung disease

- is defined as a diagnosis by a physician of a chronic lung disease (e.g. COPD, chronic bronchitis, pulmonary fibrosis) and/or their pharmacological treatment, for example, with inhalable or oral pharmaceuticals (e.g. betamimetics, anti-inflammatory drugs, leukotriene receptor antagonists, or steroids).

Primary pulmonary hypertension

- is defined as physician-diagnosed and/or treated primary pulmonary hypertension.

Depression

- is defined as a current or previous medical diagnosis of depression. The administration of antidepressants alone does not qualify for a diagnosis of depression.

Cancer more than 5 years ago

- is defined as a current or previous medical diagnosis of malignant cancer. Basal cell carcinoma is not counted as a malignancy.

Cancer within the last 5 years

- is defined as malignant cancer diagnosed by a physician less than 5 years ago. Basal cell carcinoma is not counted as a malignancy.

Other anamnestic information for women only Menopause

- is defined as the time of the last spontaneous menstrual period in the life of a woman that is not followed by ovarian triggered bleeding from the uterus for at least 12 months. The year in which the menopause began is to be coded. The day on which the last menstrual period began is required only for perimenopausal women.

PHYSICAL EXAMINATION

Blood pressure

- the systolic blood pressure should be measured using a blood pressure monitor that is serviced and calibrated on a regular basis. Where possible, devices tested for epidemiological studies (e.g. Omron 705 IT) should be used. Blood pressure measurement begins after the patient has been sitting for at least 5 minutes. Three measurements are taken at intervals of 2 minutes; the mean values of the second and third measurements are entered into the CRF.

Heart rate

- Measurement of the heart rate begins after the patient has been sitting down for at least 5 minutes. This should take place after blood pressure measurement. A manual count of the radial pulse over 30 seconds is performed; this value multiplied by two should be entered into the CRF (beats/minute).

Other diagnosis

Exertional Dyspnea

- a patient who complains of dyspnea on exertion within the last 14 days and/or at present. In cases of known heart failure, for patients within NYHA stages II-IV, dyspnea on exertion should be coded.

Dyspnea at rest

- a patient who complains of shortness of breath even when at rest (e.g. when talking) within the last 14 days and/or at present. In cases of known heart failure, for patients in NYHA stage IV, dyspnea at rest should be coded.

Peripheral edema

- a patient who complains of bilateral clinically or self-perceived water retention in the extremities within the last 14 days and/or at present.

Jugular vein congestion

- the diagnostic test for jugular vein congestion is conducted with the upper body of the patient positioned at a 45° angle. The height at which the jugular vein collapses is then determined. on-pathological collapse is no later than the level of the jugular, which usually corresponds to an 8 cm water column or 5-6 mmHg anterior to the right atrium. If the jugular vein collapses above the jugulum, jugular venous congestion must be coded.

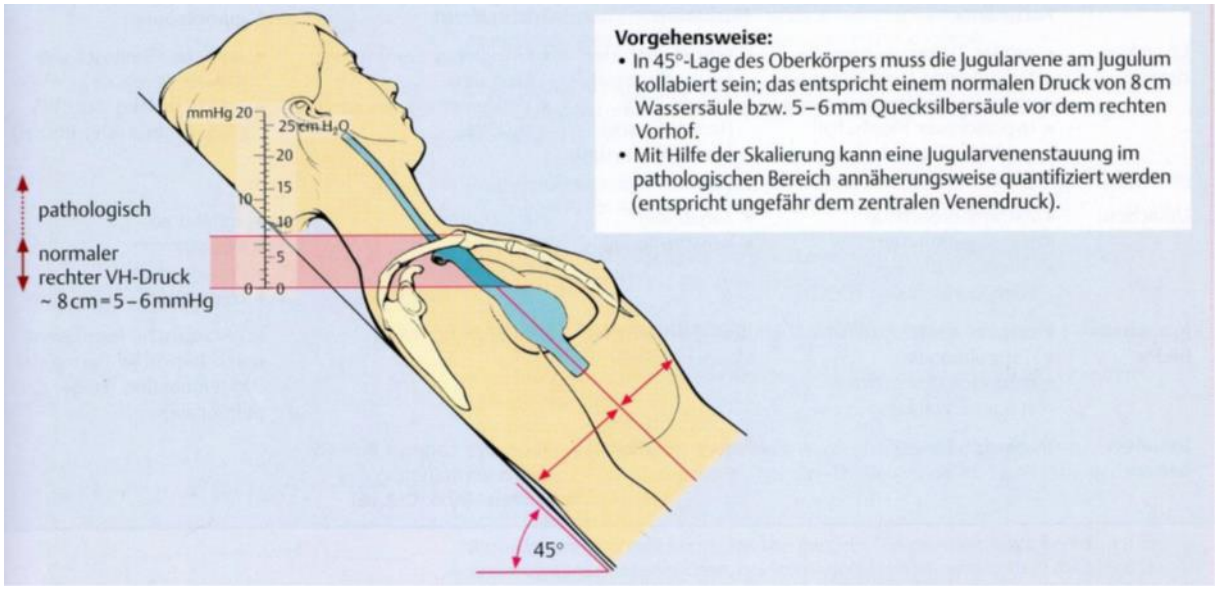


Figure 1: Diagnostic test for jugular venous congestion (CVP measurement & positioning at a 45° angle)

Pulmonary rales

- are defined as sounds heard over the lung during auscultation which are created by the movement of fluids and/or secretions during inspiration and expiration. They belong to the category of respiratory sounds that are superimposed on normal breath sounds and indicate a pathological change in the lung.

Laboratory diagnostics (blood)

- in clinically stable individuals, these values may be no more than one week old, and must be determined again thereafter.

Date of blood collection

- if known, the date of the last value should be given here.

Hemoglobin

- if the value is known, it must be given in mmol/l or g/dl.

Creatinine

- this value can be determined from serum and heparin plasma and expressed in µmol/l, nmol/ml or mg/dl.

Total cholesterol

- if the value is known, it must be given in mmol/l or mg/dl.

Vital status

- vital status (alive/deceased) must be recorded for each participating subject at the end of a study. If a subject dies before the end of the study, the time of death, as well as the cause of death (cardiovascular/non-cardiovascular) must be documented. This is usually recorded on a separate eCRF form, as it is not collected at the same time as the other baseline items.

1.6 RELATIONS TO OTHER INVESTIGATIONS

Here, the interrelationships between the individual SOP to other procedures are described.

Mandatory pretest (SOP …):	*None specified*
Recommended pretest (SOP …):	*None specified*
Pretest to be excluded (SOP):	*None specified*
Interference with other parts of the study:	*None specified*

Mandatory follow-up (SOP …):	*None specified*
Recommended follow-up (SOP …):	*None specified*

Follow-up to be excluded (SOP):	*None specified*

1.7 LEVEL OF QUALITY

Quality of the data collection method

This SOP describes a data collection method that corresponds to quality level 2 of the DZHK. A higher quality level could possibly be achieved if, for example, standardized interviews such as those used in the German National Cohort were used. Because the studies planned so far in the DZHK do not require a quality level higher than 2, initially only one SOP for that level has been drafted.

DZHK Quality Levels	
Implementation	
Level 1	The examination is performed in accordance with the guidelines of the scientific societies.
Level 2	The examination is performed in accordance with the specifications of the DZHK SOP. Minimum requirements to ensure the quality of the implementation and the investigators are defined in the SOP.
Level 3	The examination is performed in accordance with the specifications of the DZHK SOP and certification of the investigators: Definition of intra-observer and inter-observer variability (standard of epidemiological studies).

2 PREREQUISITE OF THE INVESTIGATION

All circumstances are considered in order to ensure that the examination is conducted under suitable conditions.

2.1 REQUIREMENTS FOR ROOMS/EQUIPMENT

The examination room should have a room temperature of 22-26 °C. Generally, the room should have a table at which the proband and the interviewer can sit in a comfortable atmosphere in order to conduct the interview.

2.2 EQUIPMENT/HARDWARE

PC with a monitor, keyboard, mouse, printer and printer paper. Depending on the respective study, the forms for standardized documentation of the proband's responses should be available as source files, if needed.

2.3 SPECIAL CLINICAL CONSUMABLES

None.

2.4 DOCUMENTS REQUIRED

- Docket
- Barcode for scanning

2.5 INFORMATION REQUIRED

- Examiner number
- Survey number (label)
- Beginning of examination
- Proband number

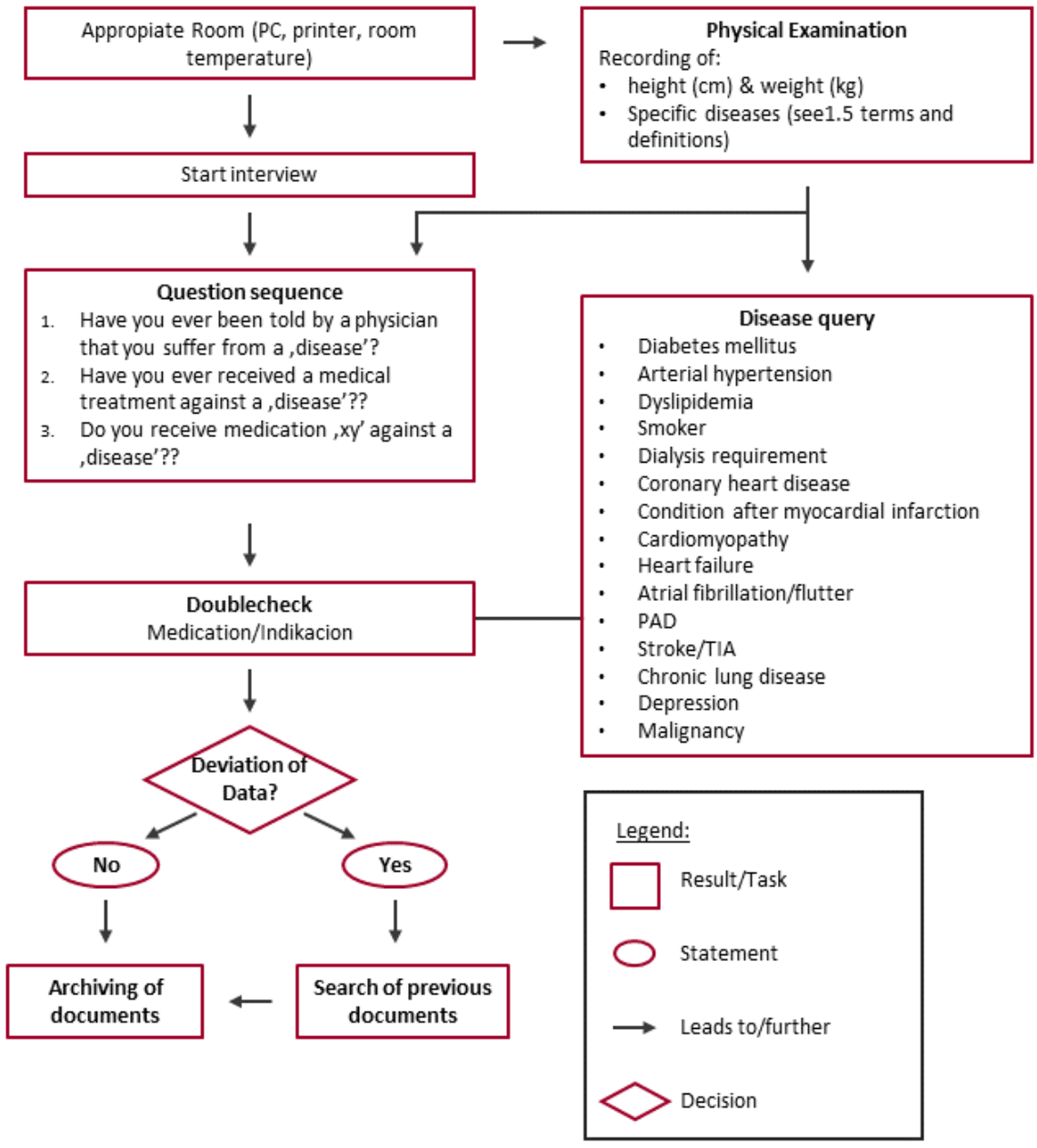
2.6 STAFF

Persons using this SOP must have completed their training in the medical field (e.g. medical assistant, nurse, licensed physician). Students of medicine may use this SOP after they have successfully passed their first medical examination (German *Physikum)*.

All users must have completed a prior course of instruction/certification for this SOP.

3 IMPLEMENTATION PROCESS/WORK PROCESS/WORK STEPS

3.1 PROCESS FLOW CHART



3.2 PREPARING FOR THE EXAMINATION

3.2.1 Preparing the Work Space

Seek a suitable room with a table. Bring the room to a temperature between 22 and 26 °C.

3.2.2 Preparing the Equipment

All equipment (PC/laptop/printer) should be switched on and must be ready for operation. A form (source data documentation) should be at hand.

3.2.3 Principles of preparation of the person to be examined

Special subject preparation is not necessary.

3.3 CARRYING OUT THE EXAMINATION

Physical examination – anthropometry

- Height (in cm) and weight (in kg) are given either as self-reported values (level 1) or as measured values (level 2). In the eCRF, a mark is made to whether the values given are based on anamnestic information or measured values.

A diagnosis is considered to be given if diagnosed by a physician and/or therapy is being administered which is considered to specifically target a certain disease. All documentation in medical documents (e.g. doctor‘s letters) justifies accepting the diagnosis as given.

When carrying out the examination, for each clinical diagnosis, the following questions should be asked in the interview:

1. Have you ever been told by a physician that you suffer from a ‘disease’?
2. Have you ever received a medical treatment against a ‘disease’?
3. Do you receive medication ‘xy’ against a ‘disease’?

As a ‘cross-check’, the indication should be requested and documented for each for each medication that the participating person receives. A validation rule will be added to the database which will produce a notification when inconsistencies arise (e.g. negative responses to questions 1-3, but the subject is taking the corresponding medication).

When uncertainties arise (e.g. as to whether the relevant diagnoses have been made, but the subject has consulted doctors for clarification), when and where those consultations took place should be noted as precisely as possible in the remarks field. If necessary, corresponding source data should be requested after the interview.

Inquiry about the following specific diseases, see section 1.5:

- Diabetes mellitus
- Arterial hypertension
- Dyslipidemia
- Smoker
- Positive family history of cardiovascular disease
- Dialysis dependency
- Coronary heart disease
- Status post myocardial infarction
- Cardiomyopathy
- Heart failure
- Atrial fibrillation/flutter
- PAOD
- Stroke/TIA
- Chronic lung disease
- Depression
- Malignancy

3.4 FOLLOW-UP AND RECORDING OF DATA

A special debriefing session is not planned. The data should be entered without delay (usually within 7 days).

3.5 DEALING WITH DEVIATIONS

If a clear answer cannot be obtained for certain questions, this should be documented.

General particularities should always be noted in the commentary/notes field.

4 LITERATURE AND REFERENCES

ACCF/AHA Guidelines Circulation 2011;124:103-123

5 MODIFICATIONS

Modifications compared with the previous version.

Section	Description of the modification compared with the previous version
1.5	Ethnic affiliation: Skin color not applicable
	Diabetes mellitus, specification of threshold values
	Dyslipidemia, specification of limit values
	Degree of renal dysfunction (grading)
	Vital status
	Laboratory diagnostics

6 LIST OF CONTRIBUTORS

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Dr. Christoph Gertler	WG Data standardization	Scientific review
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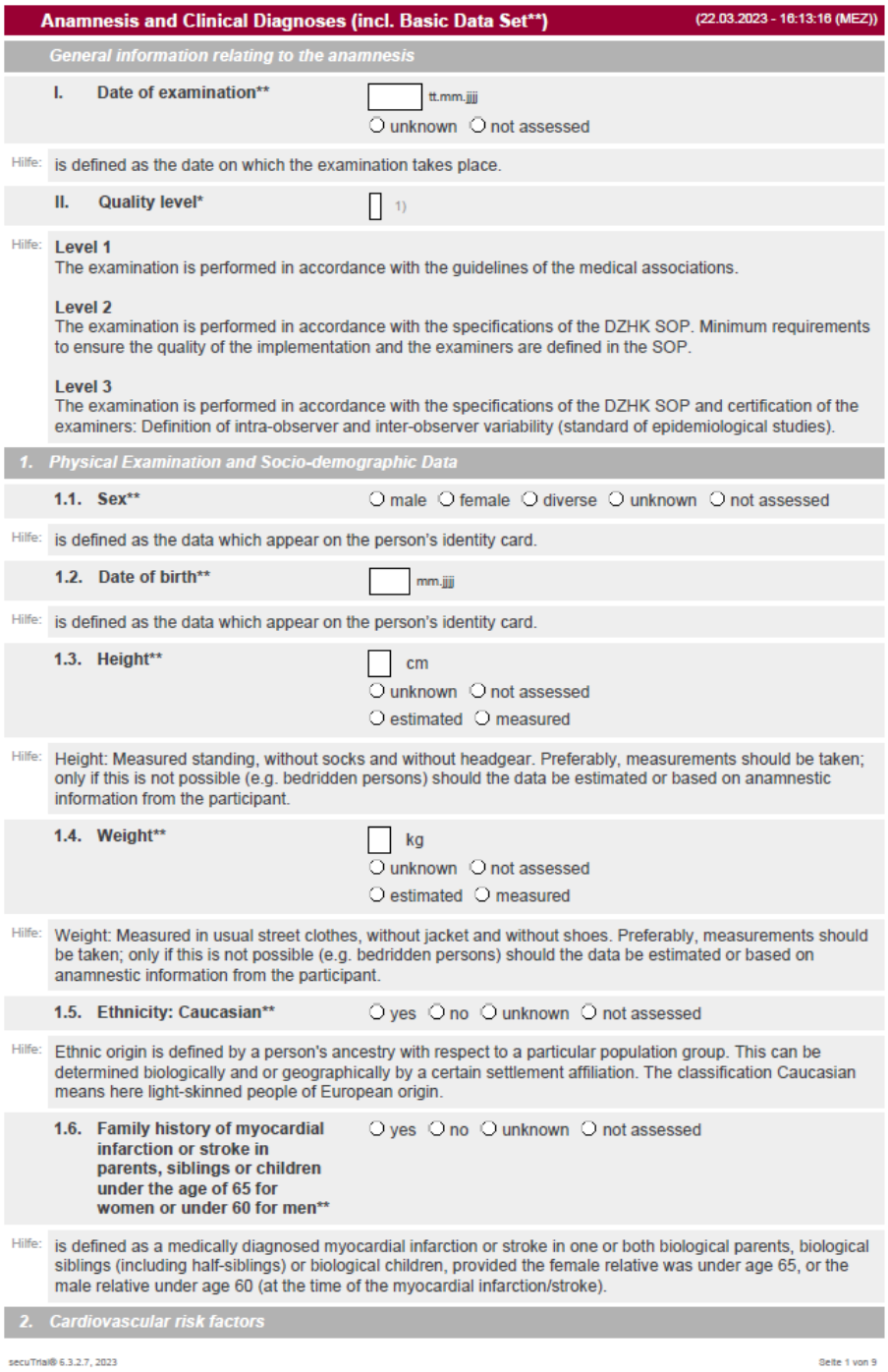
7 APPENDIX

7.1 ECRF MODULE



Anamnesis and Clinical Diagnoses (incl. Basic Data Set)** (22.03.2023 - 16:13:16 (MEZ))

General information relating to the anamnesis

I. **Date of examination**** ☐ tt.mm.jjjj
○ unknown ○ not assessed

Hilfe: is defined as the date on which the examination takes place.

II. **Quality level*** ☐ 1)

Hilfe: **Level 1**
The examination is performed in accordance with the guidelines of the medical associations.

Level 2
The examination is performed in accordance with the specifications of the DZHK SOP. Minimum requirements to ensure the quality of the implementation and the examiners are defined in the SOP.

Level 3
The examination is performed in accordance with the specifications of the DZHK SOP and certification of the examiners: Definition of intra-observer and inter-observer variability (standard of epidemiological studies).

1. Physical Examination and Socio-demographic Data

1.1. **Sex**** ○ male ○ female ○ diverse ○ unknown ○ not assessed

Hilfe: is defined as the data which appear on the person's identity card.

1.2. **Date of birth**** ☐ mm.jjjj

Hilfe: is defined as the data which appear on the person's identity card.

1.3. **Height**** ☐ cm
○ unknown ○ not assessed
○ estimated ○ measured

Hilfe: Height: Measured standing, without socks and without headgear. Preferably, measurements should be taken; only if this is not possible (e.g. bedridden persons) should the data be estimated or based on anamnestic information from the participant.

1.4. **Weight**** ☐ kg
○ unknown ○ not assessed
○ estimated ○ measured

Hilfe: Weight: Measured in usual street clothes, without jacket and without shoes. Preferably, measurements should be taken; only if this is not possible (e.g. bedridden persons) should the data be estimated or based on anamnestic information from the participant.

1.5. **Ethnicity: Caucasian**** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: Ethnic origin is defined by a person's ancestry with respect to a particular population group. This can be determined biologically and or geographically by a certain settlement affiliation. The classification Caucasian means here light-skinned people of European origin.

1.6. **Family history of myocardial infarction or stroke in parents, siblings or children under the age of 65 for women or under 60 for men**** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as a medically diagnosed myocardial infarction or stroke in one or both biological parents, biological siblings (including half-siblings) or biological children, provided the female relative was under age 65, or the male relative under age 60 (at the time of the myocardial infarction/stroke).

2. Cardiovascular risk factors

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2.1. Diabetes mellitus** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as diabetes which has been diagnosed and/or treated by a physician.
1. American Diabetes Association criteria include:
   - hemoglobin A1c ≥ 6.5 % (48 mmol/mol Hb) or a fasting blood glucose level of ≥ 126 mg/dl (7.0 mmol/l) **or** a 2-hour blood glucose level of ≥ 200 mg/dl dl (11.1 mmol/l) during an oral glucose tolerance test.

2.2. Arterial hypertension** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as a current or previous medical diagnosis of arterial hypertension, treated with diet, exercise, and/or medication. Systolic blood pressure values ≥ 140 mmHg and/or diastolic blood pressure values ≥ 90mmHg measured by a physician on at least two separate days after a 5-minute resting phase qualify for a diagnosis of arterial hypertension.

2.3. Dyslipidemia** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as a current or previous diagnosis of dyslipidemia which was diagnosed and/or is being treated by a physician.
One or more of the following criteria:
1. total cholesterol ≥ 190 mg/dl (5mmol/l),
2. LDL cholesterol ≥ 115 mg/dl (3mmol/l),
3. HDL cholesterol < 40 mg/dl (1mmol/l) (men) and < 45 mg/dl (1,2 mmol/l) (women).

2.4. Smoker** ○ yes ○ no ○ ex-smoker (stopped ≥ 6 mth. ago) ○ unknown ○ not assessed

Ex-smoker since** ☐ jjjj
○ unknown ○ not assessed

Pack years* ☐
○ unknown ○ not assessed

Hilfe: is defined as current or previous use of cigarettes, cigars, pipes, hookah, e-cigarette or smokeless tobacco.
1. ‚Yes' for daily or occasional smoking (≥ 1x/month) even with abstinence of less than 6 months;
2. ‚Ex-smoker' if abstinent for more than 6 months; ex-smoker since ...;
3. ‚No' for ‚never smoked'.
4. Pack year is the product of the number of years of cigarette smoking multiplied by the average number of packs smoked per day.
   Example: A patient who has smoked 2 packets of cigarettes per day for 20 years has 40 pack years

2.5. Drinks per week* ☐
○ unknown ○ not assessed

Hilfe: the number of alcoholic drinks consumed per week. One drink is defined as e.g. 0.25 l of beer, 0.1 l of wine or 0.02 l of spirits.
Example: A person who drinks 0.5 l beer twice a week on average has 4 drinks per week.

2.6. Medically diagnosed alcoholism** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as a current or previous physician's diagnosis of alcoholism.

2.7. Renal failure* ○ yes ○ no ○ unknown ○ not assessed

2.7.1. Degree of renal dysfunction* ○ 1 – eGFR 90 ml/min or higher
○ 2 – eGFR 60–89 ml/min
○ 3 – eGFR 30-59 ml/min
○ 4 – eGFR 15-29 ml/min
○ 5 – eGFR < 15 ml/min or current dialysis dependency
○ unknown
○ not assessed

Hilfe: any participating individual who has a renal function impairment as diagnosed by a physician.

Degree of renal dysfunction:
If known, the degree of renal dysfunction should be quantified using the estimated glomerular filtration rate

(eGFR). There are different methods for estimation, but if available, the MDRD formula should be used (s. SOP).
Based on the results, the following grade classification is made:
1 – eGFR 90 ml/min or higher
2 - eGFR 60-89 ml/min
3 - eGFR 30-59 ml/min
4 - eGFR 15-29 ml/min
5 - eGFR < 15 ml/min or current dialysis requirement
unknown
not assessed

2.8. Current dialysis dependency** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as current regular, at least weekly, renal replacement therapy (including hemodialysis and peritoneal dialysis) within the last 30 days.

3. *Cardiac Diagnoses (Anamnesis and Previous Findings)*

3.1. Coronary heart disease** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as a current or previous medical diagnosis with one or more of the following criteria:
1. coronary artery stenosis of ≥ 50 % (diagnosed by cardiac catheterization or another direct coronary artery imaging method),
2. previous coronary artery bypass operation,
3. previous percutaneous coronary intervention,
4. arteriosclerosis-induced myocardial infarction.

3.2. Condition post myocardial infarction** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is a physician's diagnosis of the disease. Rationale: Acute myocardial infarction is defined as evidence of myocardial necrosis in a clinical setting consistent with myocardial infarction.
One or more of the following criteria must apply:

1. Evidence of an increase or decrease of a cardiac biomarker (preferably troponin) with at least one value above the 99 % percentile of the upper reference limit and, additionally, at least one of the following factors:
   - Ischemic symptoms,
   - ECG changes indicative of new ischemia, e.g. ST segment changes or a new left bundle branch block, development of pathological Q waves in the ECG,
   - imaging studies show a loss of viable myocardial tissue or new regional kinetic abnormalities,
   - angiographic evidence of stenosis/vascular occlusion.

3.3. Cardiomyopathy** ○ yes ○ no ○ unknown ○ not assessed
If the response to this question is "yes", please complete the "Cardiomyopathy Diagnostics" form.

Hilfe: is defined as a physician's diagnosis of a primary heart muscle disease. If the response to this question is "yes", further data is collected in the "Cardiomyopathy Diagnostics" form.

3.4. Heart failure** ○ yes ○ no ○ unknown ○ not assessed

3.4.1. S.p. decompensation* ○ yes ○ no ○ unknown ○ not assessed

3.4.2. Initial diagnosis of heart failure* ☐ jjjj
○ unknown ○ not assessed

3.4.3. Current NYHA class* ○ I ○ II ○ III ○ IV ○ unknown ○ not assessed

Hilfe: is defined as a current or previous physician-documented diagnosis of heart failure, based on the following symptoms: shortness of breath with mild exertion, recurrent shortness of breath when sitting, fluid overload or pulmonary rales, jugular venous congestion, pulmonary edema on physical examination or pulmonary edema on chest x-rays. Documentation of reduced left ventricular function alone in the absence of clinical signs of heart failure does not meet the criteria for heart failure.
Status post decompensation is defined as any previous admission to a hospital with symptoms of heart failure (see above).

Initial diagnosis of heart failure is defined as the time point when heart failure was diagnosed for the first time by a physician. Hence, it does not refer to the time point of first onset of symptoms, which is often much earlier.
NYHA class: Classification of the patient's symptoms based on the New York Heart Association classification of heart failure:

1. NYHA I: No complaints
2. NYHA II: Complaints with greater exertion
3. NYHA III: Complaints during light exertion
4. NYHA IV: Complaints at rest

3.5. Atrial fibrillation/flutter** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as a current or previous physician's diagnosis of atrial fibrillation or atrial flutter. It is determined as persisting for at least 30 seconds or evidence on surface ECG.

3.6. Current or previous medical diagnosis of heart valve disease** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as heart valve disease (insufficiency or stenosis), which has been diagnosed and/or treated by a physician. A more precise differentiation and severity classification of valvular heart disease will be made on the echocardiography form if an echocardiogram is documented as part of the study.

3.7. Medically diagnosed endocarditis* ○ yes ○ no ○ unknown ○ not assessed

Hilfe: if at any time, currently or in their previous medical history, a person has been diagnosed with endocarditis (heart valve inflammation), it will be documented here.

3.8. Physician diagnosed congenital heart defect** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: if a patient has a known congenital heart defect, this is coded here. Congenital heart defects include shunt vitia defects (e.g. ASD, VSD), congenital valvular heart diseases (e.g. pulmonary stenosis) and cardiomyopathies diagnosed in the first five years of life. Patent foramen ovale does not belong to the class of congenital heart defects.

4. Previous cardiovascular interventions

4.1. Interventional coronary revascularization** ○ yes ○ no ○ unknown ○ not assessed

4.1.1. If yes, date of last intervention* [ ] mm.jjjj

○ unknown ○ not assessed

Hilfe: is defined as an intervention performed transcutaneously on a coronary vessel, e.g. PTCA, stent implantation, rotablation et cetera. Purely diagnostic measures (intravascular ultrasound (IVUS), optical coherence tomography (OCT)) as well as functional measurements (e.g. fractional flow reserve (FFR) measurements) are not interventional coronary revascularization procedures. Where applicable, the date of the last intervention should be entered.

4.2. Peripheral revascularization* ○ yes ○ no ○ unknown ○ not assessed

4.2.1. If yes, date of last intervention* [ ] mm.jjjj

○ unknown ○ not assessed

Hilfe: is defined as an intervention performed transcutaneously on a peripheral vessel (excluding coronary vessels or bypass grafts), e.g., PTA, stent implantation, rotablation, etc. If applicable, enter the date of the last intervention. Ablation procedures (e.g., renal denervation) are not peripheral revascularization. Where applicable, the date of the last intervention should be entered.

4.3. Coronary bypass operation** ○ yes ○ no ○ unknown ○ not assessed

4.3.1. If yes, date of last intervention* [ ] mm.jjjj

○ unknown ○ not assessed

Hilfe: is defined as surgical myocardial revascularization using bypass graft (e.g. from the mammary artery or using arterial/venous grafts). Where applicable, the date of the most recent surgery should be entered.

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4.4. Other vascular operation* ○ yes ○ no ○ unknown ○ not assessed

4.4.1. If yes, date of last intervention* ☐ mm.jjjj

○ unknown ○ not assessed

Hilfe: is defined as surgery of any kind on non-coronary vessels. Where applicable, the date of the most recent surgery should be entered.

4.5. Heart valve operation** ○ yes ○ no ○ unknown ○ not assessed

4.5.1. If yes, date of last intervention* ☐ mm.jjjj

○ unknown ○ not assessed

Hilfe: is defined as a minimally invasive percutaneous (catheter-based) or open surgical procedure on a heart valve. This includes the surgical reconstruction/replacement of heart valves, valvuloplasty procedures as well as interventional treatment of heart valve diseases (e.g. blasting, implantation of prostheses, repair of heart valves). Where applicable, the date of the most recent surgery should be entered. The most recent event is to be coded according to type, whereby any transapical aortic valve replacements are to be coded as "catheter-based". In addition, details of the surgical procedure should be given.

4.5.2. Type of last intervention* ○ open surgery ○ catheter-based ○ unknown ○ not assessed

If open surgery* ○ replacement ○ reconstruction ○ unknown ○ not assessed

4.5.3. If more than one procedure on one valve was performed, please provide details of the last OP (= current state)*

Aortic valve* ○ native ○ reconstruction ○ mechanical prosthesis ○ bioprosthesis (open) ○ TAVI ○ unknown ○ not assessed

○ transfemoral ○ transapical ○ transaortal ○ unknown ○ not assessed

Pulmonic valve* ○ native ○ reconstruction ○ mechanical prosthesis ○ bioprosthesis (open) ○ unknown ○ not assessed

Mitral valve* ○ native ○ reconstruction ○ mechanical prosthesis ○ bioprosthesis (open) ○ clipping ○ unknown ○ not assessed

Triscuspid valve* ○ native ○ reconstruction ○ mechanical prosthesis ○ bioprosthesis (open) ○ unknown ○ not assessed

4.6. Implantable pacemaker or defibrillator** ○ yes ○ no ○ unknown ○ not assessed

4.6.1. If yes, what was implanted?* ○ pacemaker ○ defibrillator ○ unknown ○ not assessed

4.6.2. If yes, date of last event (implantation/exchange)* ☐ mm.jjjj

○ unknown ○ not assessed

4.6.3. If pacemaker, please give pacemaker type* ○ 1-chamber pacemaker (e.g. VVI) ○ 2-chamber pacemaker (e.g. DDD) ○ biventricular pacemaker (CRT) ○ unknown ○ not assessed

Hilfe: is defined as condition after implantation of a pacemaker or intracardiac defibrillator (ICD). Where applicable, the date of the most recent operation (implantation/exchange) is toshould be entered. The number of probes currently connected to the pacemaker device is also coded. A device with only one probe is to be coded as a 1-chamber pacemaker, a device with atrial and ventricular probes as a 2-chamber pacemaker. Devices for cardiac resynchronization therapy, with two ventricular probes, are to be coded as a biventricular pacemaker (CRT).

4.7. Other devices* ○ yes ○ no ○ unknown ○ not assessed

4.7.1. Cardiac contractility modulation (CCM)* ○ yes ○ no ○ unknown ○ not assessed

4.7.2.	**Intra-aortic balloon pump (IABP)***	○ yes ○ no ○ unknown ○ not assessed
4.7.3.	**Other devices***	

Hilfe: are defined as other implantable devices for cardiac/vascular support. This includes devices for cardiac contractility management, for neuromodulation (e.g. vagus nerve stimulator, baroreceptor stimulator), intra-aortic balloon pumps and left ventricular cardiac assist devices.

4.8.	**S.p. myocardial biopsy***	○ yes ○ no ○ unknown ○ not assessed
4.8.1.	**Date of myocardial biopsy***	☐ mm.jjjj ○ unknown ○ not assessed
4.8.2.	**Biopsy sites***	○ left ventricle ○ right ventricle ○ left and right ventricle ○ unknown ○ not assessed

Hilfe: is defined as status post bioptic removal of tissue from the myocardium (e.g. during a right/left catheter examination or surgery). Where applicable, the sampling site as well as the date of the most recent myocardial biopsy should be coded.

5. *Current secondary diagnoses*

5.1.	**PAOD****	○ yes ○ no ○ unknown ○ not assessed
5.1.1.	**Fontaine stage***	○ I ○ IIa ○ IIb ○ III ○ IV ○ unknown ○ not assessed
5.1.2.	**Acute ischaemic occlusion***	○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as a current or previous diagnosis by a physician of peripheral arterial occlusive disease (pelvic-leg vessels or upper extremity from the subclavian artery to distal). Renal, coronary, cerebral and mesenteric vessels and aneurysms are excluded. Possible symptoms are:

1. intermittent claudication,
2. pain at rest,
3. amputation due to severe arterial vascular insufficiency,
4. vascular reconstruction, bypass surgery or percutaneous revascularization,
5. a positive non-invasive test (e.g. ankle-brachial index of ≤ 0.9, pathological TCPO2 measurement, evidence of 50 % or greater stenosis of a peripheral artery by Doppler/duplex sonography, CT, MRT, or angiography).

Classification of the degree of severity is done according to the Fontaine classification:

Stage and Clinical Picture	
I.	Asymptomatic PAOD
II.	Intermittent claudication 1. with walking distances > 200 metres (Stage IIa) 2. with walking distances < 200 metres (Stage IIb)
III.	Pain at rest
IV.	Necrosis, gangrene

Acute ischemic occlusion refers to a currently (in the last 30 days) occurring proven acute ischemic occlusion of a peripheral arterial vessel.

5.2.	**Stroke/TIA****	○ yes ○ no ○ unknown ○ not assessed
5.2.1.	**Date***	☐ mm.jjjj ○ unknown ○ not assessed
5.2.2.	**Aetiology***	○ ischaemic ○ haemorrhagic ○ unknown ○ not assessed
5.2.3.	**Diagnosis***	○ TIA ○ stroke ○ unknown ○ not assessed
5.2.4.	**Stroke severity***	○ minor ○ major ○ unknown ○ not assessed
5.2.5.	**Consequences of the stroke***	○ disabling ○ non-disabling ○ unknown ○ not assessed

Hilfe: is defined as a current or previous diagnosis by a physician of:

1. Ischaemic stroke: Infarction of tissue of the central nervous system, either symptomatic or silent (asymptomatic).
2. Transient ischaemic attack (TIA): A transient episode of neurological dysfunction caused by focal cerebral, spinal cord or retinal ischaemia without acute infarction, which resolves completely within 24 hours. This definition is not met by chronic (non-vascular) neurological diseases or other acute neurological diseases such as metabolic or ischaemic encephalopathy resulting from general hypoxia (e.g. respiratory failure, post cardiovascular arrest).
3. Haemorrhagic stroke: Neurological dysfunction caused by intra-cranial bleeding.
4. Stroke where there is uncertainty as to whether the cause was haemorrhagic or ischaemic.

Severity of the stroke: A stroke is considered "minor" if neurological symptoms can be completely reversed within 30 days or the change in the NIH Stroke Scale (see Appendix 7.3 NIH Stroke Scale) is less than 3 points compared to the NIH Stroke Scale before the stroke. A stroke is considered "major" if neurological deficits are still detectable 30 days after the event or the NIH Stroke Scale is at least 3 points higher than prior to the stroke.

Consequences of the stroke: A stroke is considered "disabling" if the modified Ranking Scale score is greater than 2 90 days after the stroke. If the modified Rankin Scale score is 2 points or less 90 days after the stroke, the stroke is coinsidered "non-disabling".

The modified Rankin Scale of 0 to 6 describes the range from complete health to death.

5. 0 - No symptoms.
6. 1 - No significant impairment. Can perform daily activities despite some symptoms.
7. 2 - Slight impairment. Is able to care for him or herself without assistance, but is limited in daily activities.
8. 3 - Moderate impairment. Requires assistance in daily life, but is able to walk without assistance.
9. 4 - More severe impairment. Requires assistance with personal hygiene; is not able to walk without assistance.
10. 5 - Severe impairment. Bedridden, incontinent, requires constant nursing assistance.
11. 6 – Death caused by apoplexy.

5.3. Chronic lung disease** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as a diagnosis by a physician of a chronic lung disease (e.g. COPD, chronic bronchitis, pulmonary fibrosis) and/or their pharmacological treatment, for example, with inhalable or oral pharmaceuticals (e.g. betamimetics, anti-inflam¬matory drugs, leukotriene receptor antagonists, or steroids).

5.4. Primary pulmonary Hypertension* ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as physician-diagnosed and/or treated primary pulmonary hypertension.

5.5. Depression** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as a current or previous medical diagnosis of depression. The administration of antidepressants alone does not qualify for a diagnosis of depression.

5.6. Cancer more than 5 years ago** ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as a current or previous medical diagnosis of malignant cancer. Basal cell carcinoma is not counted as a malignancy.

5.7. Cancer within the last 5 years* ○ yes ○ no ○ unknown ○ not assessed

Hilfe: is defined as malignant cancer diagnosed by a physician less than 5 years ago. Basal cell carcinoma is not counted as a malignancy.

6. Blood pressure after 5 minutes at rest

6.1. Systolic** ☐ mmHg ○ unknown ○ not assessed

6.2. Diastolic** ☐ mmHg ○ unknown ○ not assessed

Hilfe: The systolic blood pressure should be measured using a blood pressure monitor that is serviced and calibrated on a regular basis. Where possible, devices tested for epidemiological studies (e.g. Omron 705 IT) should be

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used. Blood pressure measurement begins after the patient has been sitting for at least 5 minutes. 3Three measurements are taken at intervals of 2 minutes; the mean values of the second and third measurements are entered into the CRF.

7. Heart rate after sitting down for 5 minutes

7.1. Heart rate**

☐ per minute

○ unknown ○ not assessed

Hilfe: Measurement of the heart rate begins after the patient has been sitting down for at least 5 minutes. This should take place after blood pressure measurement. A manual count of the radial pulse over 30 seconds is performed; this value multiplied by two should be entered into the CRF (beats/minute).

8. Other diagnosis

8.1. Exertional Dyspnea*

○ yes ○ no ○ unknown ○ not assessed

Hilfe: A patient who complains of dyspnea on exertion within the last 14 days and/or at present. In cases of known heart failure, for patients within NYHA stages II-IV, dyspnea on exertion should be coded.

8.2. Dyspnea at rest*

○ yes ○ no ○ unknown ○ not assessed

Hilfe: A patient who complains of shortness of breath even when at rest (e.g. when talking) within the last 14 days and/or at present. In cases of known heart failure, for patients in NYHA stage IV, dyspnea at rest should be coded.

8.3. Peripheral edema*

○ yes ○ no ○ unknown ○ not assessed

Hilfe: A patient who complains of bilateral clinically or self-perceived water retention in the extremities within the last 14 days and/or at present.

8.4. Jugular venous distention*

○ yes ○ no ○ unknown ○ not assessed

Hilfe: The diagnostic test for jugular vein congestion is conducted with the upper body of the patient positioned at a 45° angle. The height at which the jugular vein collapses is then determined. on-pathological collapse is no later than the level of the jugular, which usually corresponds to an 8 cm water column or 5-6 mmHg anterior to the right atrium. If the jugular vein collapses above the jugulum, jugular venous congestion must be coded.

8.5. Pulmonary rales*

○ yes ○ no ○ unknown ○ not assessed

Hilfe: are defined as sounds heard over the lung during auscultation which are created by the movement of fluids and/or secretions during inspiration and expiration. They belong to the category of respiratory sounds that are superimposed on normal breath sounds and indicate a pathological change in the lung.

9. Laboratory diagnostics (blood)

In clinically stable individuals, these values may be no more than one week old, and must be determined again thereafter.

9.1. Date blood sample was taken**

☐ tt.mm.jjjj Where applicable, give date for the latest value

○ unknown ○ not assessed

Hilfe: if known, the date of the last value should be given here.

9.2. Hemoglobin**

☐

○ unknown ○ not assessed

Unit**

○ mmol/l

○ g/dl

Hilfe: if the value is known, it must be given in mmol/l or g/dl.

9.3. Creatinine (serum, heparin plasma)**

☐

○ unknown ○ not assessed

Unit**

○ µmol/l=nmol/ml

○ mg/dl

Hilfe: this value can be determined from serum and heparin plasma and expressed in µmol/l, nmol/ml or mg/dl.

9.4. Total cholesterol**

☐

○ unknown ○ not assessed

Unit**

○ mmol/l
○ mg/dl

Hilfe: if the value is known, it must be given in mmol/l or mg/dl.

10. The next three anamnestic questions are for women only

10.1. Menopause?**

○ yes ○ no ○ unknown ○ not assessed

10.1.1 Year of menopause**

☐ jjjj

○ unknown ○ not assessed

10.2. Day last menstrual period began**

☐ tt.mm.jjjj

○ unknown ○ not assessed

Hilfe: is defined as the time of the last spontaneous menstrual period in the life of a woman that is not followed by ovarian triggered bleeding from the uterus for at least 12 months.. The year in which the menopause began is to be coded. The day on which the last menstrual period began is required only for perimenopausal women.

Mögliche Angaben

Bitte wählen Sie bei den oben mit Anmerkungen versehenen Feldern eine der hier aufgelisteten Angaben.

1)

1
2
3

Vital status		(22.03.2023 - 16:13:16 (MEZ))
1.	Was the vital status recorded?**	○ yes ○ no ○ unkown ○ not assessed
2.	Date of last contact**	tt.mm.jjjj
3.	Status of the patient**	○ is alive ○ is dead
4.	Date of death**	tt.mm.jjjj
5.	Cause of death**	○ cardiovascular ○ non-cardiovascular ○ unknown ○ not assessed

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7.2 DEFINITION OF CARDIOMYOPATHIES FROM TORCH REGISTRY

7.2.1 Definition of cardiomyopathies included in the registry

7.2.1.1 Definition of hereditary dilated cardiomyopathy

The definition of hereditary dilated cardiomyopathy (DCM) is established for DZHK TORCH and has been adopted from the following indications:

- study of familial dilated cardiomyopathies provided by the Collaborative Research Group of the European Human and Capital Mobility Project on Familial Dilated Cardiomyopathy in 1999
- and the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases position statement on the Classification of the cardiomyopathies in 2008

For the purpose of our registry, these recommendations have been updated in regards to imaging modalities used for characterization and the range of exclusion criteria.

DCM is defined by the presence of both left ventricular dilatation and left ventricular systolic dysfunction in the absence of abnormal loading conditions (hypertension, valve disease) or relevant coronary artery disease sufficient to cause global systolic impairment. Right ventricular dilation and dysfunction may be present but are not necessary to establish the diagnosis.

Major criteria

Dilatation: Left ventricular end-diastolic diameter (LVEDD) > 117 % of the predicted value corrected for age and body surface area [Henry-Formel (LVEDD= 45.3 * BSA1/3 – 0.03*Age –7.2) as ascertained by echocardiography or MRI.

Systolic dysfunction: Ejection fraction (EF) of the left ventricle <45% as ascertained by echocardiography or MRI.

Minor criteria

- Unexplained supraventricular (atrial fibrillation or sustained arrhythmias) or ventricular arrhythmias, frequent (>1000 . 24 h"1) or repetitive (three or more beats with >120 beats min"1) before the age of 50
- Left ventricular dilatation >112% of the predicted value
- Left ventricular dysfunction: ejection fraction <50%
- Unexplained conduction disease: II or III atrioventricular conduction defects, complete left-ventricular bundle branch block, sinus nodal dysfunction
- Unexplained sudden death or stroke before 50 years of age

- Segmental wall motion abnormalities (<1 segment, or 1 if not previously present) in the absence of intraventricular conduction defect or ischaemic heart disease.
- Elevated NTproBNP: In patients presenting with non-acute dyspnea (> 14 days), a value exceeding 125 ng/L (age < 75 years) or 450 ng/L (> 75 years) is considered abnormal. In patients with acute dyspnea or signs of heart failure, a value below 300 ng/L excludes acute heart failure (age-independent rule-out). An age-dependent value exceeding 900 ng/L (<50 years), 1,200 ng/L (50-69 years) or 1,800 ng/L (>70 years) is considered abnormal. Values between rule-out and age-dependent rule-in cutoff are called greyzone values and merit attention. Cut-off for BNP are different and are not dependent on age or gender. A value > 35 ng/L is considered abnormal for non-acute presentation, and 100 ng/L for acute manifestation.
- Data for cardiac troponins are less established: Detectable cTn concentrations are associated with midterm and longterm adverse outcomes. For hscTn hazard for death and hospitalization for heart failure has been reported to start below the 99th percentile value. A value > 99th percentile, e.g. 14 ng/L for hscTnT is definitely elevated and presumably of prognostic importance.
- Cardiac limitation during spiroergometry:
    - peakVO2 > 85% predicted value
    - VO2 at anaerobic threshold (AT) < 40% predicted VO2
    - Breathing Reserve (BR) ≥ 30% (at least ≥ 15 L/min)
    - Heart Rate Reserve (HRR) > 15/min
    - Aerobic Capacity (dVO2/dWR) ≤ 8 mL/min*W
    - Relative Dead Space Ventilation (VD/VT) ≤ 35% at rest and exercise

Exclusion criteria

- Pre-existing other cardiac diseases such as significant valvular, congenital, ischemic or pericardial diseases
- Severe arterial hypertension (RR> 160/100mmHg or hypertension despite therapy with at least 3 different drugs)
- Primary pulmonary artery hypertension
- Chronic advanced disorders requiring treatment or being the predominant clinical finding on initial presentation (rheumatic, autoimmune, malignancy, insulin dependent DM, endocrine, ESDR, liver failure, etc.)
- History of treatment with cardiotoxic agents and radiation
- Drug and alcohol abuse

Categorization, which will be applied in the registry:

- Definite DCM: An individual is defined as definitely affected in the presence of both major or left ventricular dilatation (>117%) plus one minor criterion or three minor criteria – without the presence of an exclusion criterion.

- Probable DCM: An individual is defined as probably affected in the presence of left ventricular dilatation (>112% of the predicted value) and left ventricular dysfunction (ejection fraction <50%) – without the presence of an exclusion criterion.
- Possible DCM: An individual is defined as possibly affected in the presence of left ventricular dysfunction (ejection fraction <50%) – without the presence of an exclusion criterion.

See references no. 41-45

7.2.1.2 Clinical and biopsy-based definition of inflammatory dilated cardiomyopathy and acute myocarditis

The definitions of inflammatory dilated cardiomyopathy (DCMi) and acute myocarditis established for DZHK TORCH have been adopted from:

- the 1995 Report of the World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of Cardiomyopathies,
- the World Heart Federation consensus conferences' definition of inflammatory cardiomyopathy (myocarditis) in 1999 (Marburg Classification) and from
- the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases position statement on the Classification of the cardiomyopathies in 2008.

Myocardial inflammation (autoimmune, viral, or postviral) is mediated by the effector cells of the immune system. In contrast to active myocarditis, which is by definition

- an acute inflammatory disorder
- with inflammatory cell associated myocyte necrosis of the heart
- with often preserved left ventricular size

The inflammatory DCM is defined as follows:

- the presence of inflammatory cells in association
- with left ventricular dilatation and
- reduced systolic function (dilatation and systolic function analog to definition of hereditary or post-inflammatory/infectious DCM).

Histology and/or immunocytochemistry are required for the diagnosis. A proportion of individuals with inflammatory DCM have persistence of viral genomes or proteins in the myocardium. (The term viral persistence in DCM should only be applied in those cases, in which viral RNA or DNA but no inflammation is present.) Viral persistence can be associated with or without inflammation.

World Health Organization Marburg Classification

First biopsy:

- Acute/active myocarditis: a clear-cut infiltrate (diffuse, focal or confluent) of >14 leukocytes/mm^2 (preferably activated T cells). The amount of the infiltrate should be quantified by immunohistochemistry. Necrosis or degeneration is compulsory; fibrosis may be absent or present and should be graded.
- Chronic myocarditis (histologically described as borderline myocarditis): an infiltrate of >14 leukocytes/mm^2 (diffuse, focal or confluent, preferably activated T cells). Quantification should be made by immunohistochemistry. Necrosis or degeneration is usually not evident; fibrosis may be absent or present and should be graded.
- No myocarditis: No infiltrating cells or <14 leukocytes/mm^2.

Subsequent biopsies: (histology and immunohistochemistry)

- Ongoing (persistent) myocarditis. Criteria as in active or chronic myocarditis.
- Resolving (healing) myocarditis. Criteria as in acute or chronic myocarditis, but the immunologic process is sparser than in the first biopsy.
- Resolved (healed) myocarditis. Corresponds to the Dallas classification and the immunohistochemical evaluation.

The amount and distribution of fibrosis should be described similarly as no (grade 0), mild (grade 1), moderate (grade 2), or severe (grade 3). Localisation or formation of fibrosis should be outlined as endocardial, replacement or interstitial.

Expanded criteria for clinical and biopsy-based diagnosis of myocarditis

- Suspicious for myocarditis = 2 positive categories
- Compatible with myocarditis = 3 positive categories
- High probability of being myocarditis = all 4 categories positive.
- Definite proof of myocardial inflammation and/or viral infection demands biopsy analysis (positive category 4)

NOTE: Any matching feature in category = positive for category; the categories I-III define the clinical diagnosis of myocarditis/inflammatory CMP only. A definite proof demands biopsy analysis (positive for category IV).

Category I: clinical symptoms

- Clinical heart failure
- Fever
- Viral prodrome
- Fatigue

- Dyspnea on exertion
- Chest pain
- Palpitations
- Pre-syncope or syncope

Category II: clinical evidence of cardiac structural/functional perturbation in the absence of regional coronary ischaemia

- Echo evidence
- Regional wall motion abnormalities
- Cardiac dilation
- Regional cardiac hypertrophy
- Troponin release
- Troponin result has high sensitivity (>0.1 nanogram/mL)
- Positive indium-111 antimyosin scintigraphy and normal coronary angiography or absence of reversible ischaemia by coronary distribution on perfusion scan

Category III: cardiac MRI

- Increased myocardial T2 signal on inversion recovery sequence
- Delayed contrast enhancement following gadolinium-diethylenetriamine pentaacetic acid (DTPA) infusion.

Category IV: myocardial biopsy, pathologic or molecular analysis as definite proof of myocardial inflammation and viral infection

- Pathology findings compatible with Dallas criteria supplemented by immunohistochemistry
- Presence of viral genome by PCR or in situ hybridisation.

See references no. 46-51

7.2.1.3 Definition of hypertrophic cardiomyopathy

The definition of hypertrophic cardiomyopathy (HCM) and in specific, hypertrophic obstructive cardiomyopathy (HOCM) established for DZHK TORCH has been adopted from the American/European Consensus Document on Hypertrophic Cardiomyopathy in 2003 referenced below. For the purpose of our registry, these recommendations have been updated in regards to imaging modalities used for characterization and in regards to the range of exclusion criteria.

Evidence of left ventricular hypertrophy and/or increased left ventricular mass.

Definition of hypertrophy:

- Wall thickness (including asymmetric hypertrophy in individual segments) ≥15mm
- septal/posterior wall thickness ratio >1.3 in normotensive patients, or
- septal/posterior wall thickness ratio >1.5 in hypertensive patients.

Exclusion criteria:

Hemodynamic stressors sufficient to explain hypertrophy

- systemic arterial hypertension
- Valvular disease
- athlete's heart

Systemic storage disorders

- Amyloidosis
- Glycogen storage disease
- Anderson-Fabry disease

Categorization which will be applied in the registry:

- Definite HCM: An individual is defined as definitely affected in the presence of left ventricular hypertrophy as stated above and/or increased left ventricular mass between ≥122 g/m² (women) and ≥149 g/m² (men) and impaired longitudinal function – without the presence of an exclusion criterion.
- Probable HCM: An individual is defined as probably affected in the presence of left ventricular hypertrophy with a wall thickness (including asymmetric hypertrophy in individual segments) between 11 – 14 mm (women) and 12 – 14 mm (men) and/or increased left ventricular mass between 109-121 g/m² (women) and 132-148 g/m² (men) and impaired longitudinal function – without the presence of an exclusion criterion.
- Possible HCM: An individual is defined as probably affected in the presence of left ventricular hypertrophy with a wall thickness (including asymmetric hypertrophy in individual segments) between 10 – 11 mm (women) and 11 – 12 mm (men) and/or increased left ventricular mass between 96-108 g/m² (women) and 116-131 g/m² (men) and impaired longitudinal function – without the presence of an exclusion criterion.

Specific: Hypertrophic obstructive cardiomyopathy

Evidence of HCM according to criteria listed above

AND

- Evidence of a significant left ventricular outflow tract obstruction (gradient ≥ 30 mmHg) at rest during stable pre-/afterload
- Evidence of a significant dynamic left ventricular outflow tract obstruction (gradient ≥50mmHg) (either during exercise, after glyceryl trinitrate (GTN) administration, or the Valsalva maneuver) during stable pre-/afterload

Specific: Suspected familial HCM

In family members of a HCM index patient, the following criteria are applied to define suspected HCM cases (1 major or 2 minor echocardiographic criteria, or 1 major echocardiographic criterion and 2 minor electrocardiographic criteria).

European Echo criteria	**European ECG criteria**
Major: - MWT ≥ 13mm anteroseptal or posterior - MWT ≥ 15mm posteroseptal, lateral or severe SAM	**Major:** - Abnormal Q-waves ≥ 2 leads - T-wave Inversion ≥ 2 leads - LV hypertrophy signs
Minor: - MWT ≥ 12mm anteroseptal or posterior - MWT ≥ 14mm posteroseptal, lateral or moderate SAM	**Minor:** - deep S in lead V2 - repolarization changes - bundle brunch blockage

MWT = *„myokardial wall thickness“*; SAM = *„systolic anterior motion“*

See references no. 52-69

7.2.1.4 Definition of left ventricular non-compaction cardiomyopathy

For the lack of common standardized diagnostic criteria for the left ventricular non-compaction cardiomyopathy (LVNC), following definition was established for DZHK TORCH according to the published studies.

To prevent over diagnosing of LVNC the results by echocardiography and cardiac MRI must be concordant.

Diagnosis is considered definite when the following criteria are present:

1. Absence of congenital heart disease, infiltrative/hypertrophic cardiomyopathy or documented coronary artery disease
2. Echocardiographic diagnostic features

According to Stöllberger et al.: More than three confirmed trabeculations within one image plane, apical to the insertion of the papillary muscles. Trabeculations with the same echogenicity as the myocardium and synchronous movement with ventricular contractions. Perfusion of the intertrabecular spaces from the left ventricular cavity. Ratio of compacted to non-compacted segment at least 1:2 (≤ 0.5). Acquisition of the images: apical four chamber view and three chamber view; angulation of the transducer and acquisition of pictures in atypical views to obtain the technically best picture quality for differentiation between false chords/aberrant bands and trabeculations.

3. MRI diagnostic features

Petersen et al.: Ratio between the non-compacted and compacted layer > 2.3. Measurement: at end-diastole.

See references no. 70-76

7.2.1.5 Definition of arrhythmogenic right ventricular cardiomyopathy

The definitions of arrhythmogenic right ventricular cardiomyopathy (ARVC), also called arrhythmogenic right ventricular dysplasia (ARVD), established for DZHK TORCH have been adopted from criteria described in the 2010 revised Task Force Criteria by Marcus et al. (Original International Task Force criteria from the European Society of Cardiology and the International Society and Federation of Cardiology published in 1994).

Presence of ARVC/ARVD is established following the combination of the below listed criteria as:

- definite:
  - two major criteria, or
  - one major plus two minor criteria, or
  - four minor criteria

  with each criterion being from a different category
- borderline:
  - one major and one minor, or
  - three minor criteria

  with each criterion being from a different category
- possible:
  - one major, or
  - two minor criteria

  with the criteria being from a different category

I. Global or regional dysfunction and structural alterations

Major

By 2D echo:

• Regional RV akinesia, dyskinesia, or aneurysm *and* 1 of the following (end diastole):

- PLAX RVOT ≥32 mm (corrected for body size [PLAX/BSA] ≥19 mm/m^2)
- PSAX RVOT ≥36 mm (corrected for body size [PSAX/BSA] ≥21 mm/m^2)
- *or* fractional area change ≤33 percent

By MRI:

• Regional RV akinesia or dyskinesia or dyssynchronous RV contraction *and* 1 of the following:

- Ratio of RV end-diastolic volume to BSA ≥110 mL/m^2 (male) or ≥100 mL/m^2 (female)
- *or* RV ejection fraction ≤40 percent

By RV angiography:

• Regional RV akinesia, dyskinesia, or aneurysm

Minor

By 2D echo:

• Regional RV akinesia or dyskinesia *and* 1 of the following (end diastole):

- PLAX RVOT ≥29 to <32 mm (corrected for body size [PLAX/BSA] ≥16 to <19 mm/m^2)
- PSAX RVOT ≥32 to <36 mm (corrected for body size [PSAX/BSA] ≥18 to <21 mm/m^2)
- *or* fractional area change >33 percent to ≤40 percent

By MRI:

• Regional RV akinesia or dyskinesia or dyssynchronous RV contraction *and* 1 of the following:

- Ratio of RV end-diastolic volume to BSA ≥100 to <110 mL/m^2 (male) or ≥90 to <100 mL/m^2 (female)
- *or* RV ejection fraction >40 percent to ≤45 percent

II. Tissue characterization of wall

Major

• Residual myocytes <60 percent by morphometric analysis (or <50 percent if estimated), with fibrous replacement of the RV free wall myocardium in ≥1 sample, with or without fatty replacement of tissue on endomyocardial biopsy

Minor

• Residual myocytes 60 percent to 75 percent by morphometric analysis (or 50 percent to 65 percent if estimated), with fibrous replacement of the RV free wall myocardium in ≥1 sample, with or without fatty replacement of tissue on endomyocardial biopsy

III. Repolarization abnormalities

Major

• Inverted T waves in right precordial leads (V_1, V_2, and V_3) or beyond in individuals >14 years of age (in the absence of complete right bundle-branch block QRS ≥120 ms)

Minor

• Inverted T waves in leads V_1 and V_2 in individuals >14 years of age (in the absence of complete right bundle-branch block) or in V_4, V_5, or V_6

• Inverted T waves in leads V_1, V_2, V_3, and V_4 in individuals >14 years of age in the presence of complete right bundle-branch block

IV. Depolarization/conduction abnormalities

Major

• Epsilon wave (reproducible low-amplitude signals between end of QRS complex to onset of the T wave) in the right precordial leads (V_1 to V_3)

Minor

• Late potentials by SAECG in ≥1 of the following 3 parameters in the absence of a QRS duration of ≥110 ms on the standard ECG

- Filtered QRS duration (fQRS) ≥114 ms
- Duration of terminal QRS <40 µV (low-amplitude signal duration) ≥38 ms
- Root-mean-square voltage of terminal 40 ms ≤20 µV

• Terminal activation duration of QRS ≥55 ms measured from the nadir of the S wave to the end of the QRS, including R', in V_1, V_2, or V_3, in the absence of complete right bundle-branch block

V. Arrhythmias

Major

• Nonsustained or sustained ventricular tachycardia of left bundle-branch morphology with superior axis (negative or indeterminate QRS in leads II, III, and aVF and positive in lead aVL)

Minor

• Nonsustained or sustained ventricular tachycardia of RV outflow configuration, left bundle-branch block morphology with inferior axis (positive QRS in leads II, III, and aVF and negative in lead aVL) or of unknown axis

• >500 ventricular extrasystoles per 24 hours (Holter)

VI. Family history

Major

• ARVC/D confirmed in a first-degree relative who meets current Task Force criteria

• ARVC/D confirmed pathologically at autopsy or surgery in a first-degree relative

• Identification of a pathogenic mutationΔ categorized as associated or probably associated with ARVC/D in the patient under evaluation

Minor

• History of ARVC/D in a first-degree relative in whom it is not possible or practical to determine whether the family member meets current Task Force criteria

• Premature sudden death (<35 years of age) due to suspected ARVC/D in a first-degree relative

• ARVC/D confirmed pathologically or by current Task Force Criteria in second-degree relative

See references nr. 77-78

7.2.1.6 Definitions for biopsy diagnosis of cardiomyopathies

Active Myocarditis:

Infiltrating lymphocytes (CD3) and/or monocytes/macrophages (CD68 in paraffin fixed tissues, CD11b in unfixed/frozen tissues) + inflammatory cell associated myocyte necrosis. Focally or diffusely enhanced expression of cell adhesion molecules.

Specific disease entities:

Giant cell myocarditis, eosinophilic myocarditis, granulomateous myocarditis (e.g. sarcoidosis)

Borderline-Myocarditis/inflammatory cardiomyopathy:

>14 infiltrating leukocytes with up to 4 monocytes/mm^2 with the presence of CD 3 positive T-lymphocytes ≥7 cells/mm^2 or > 35 monocytes/macrophages (CD68 in paraffin fixed tissues, CD11b in unfixed/frozen tissues) without inflammatory cell associated myocyte necrosis in addition to an enhanced expression of cell adhesion molecules (HLA-1 or HLA-DR, CD54/ICAM-1, CD106/VCAM-1)

or

Focal infiltrates of inflammatory cells (lymphocytes, monocytes/macrophages, leukocytes) in histologically (paraffin) or immunohistologically (frozen) stained tissues.

No Myocarditis/DCM:

Cell numbers of infiltrating lymphocytes or monocytes/macrophages are below those defining Borderline-Myocarditis or inflammatory CMP; a mildly enhanced expression of cell adhesion molecules (HLA-I/-DR and CD54/ICAM-1) may be present in postinflammatory tissues (resolved inflammatory cell infiltrates).

No focal inflammatory cell infiltrates in histologically or immunohistochemically analyzed tissues

Histology: cardiomyocyte hypertrophy, interstitial fibrosis, and scars may be present and indicate progressive disease

Viral myocarditis/cardiomyopathy:

Positive proof of viral genomes (PCR) with or without myocardial inflammation. Consideration of virus subtypes, virus loads, and replicative intermediates (mRNA) indicating active/recent infection or virus reactivation (myocardial tissue, blood).

HCM:

Often no specific histological or immunohistochemical features, since endomyocardial biopsy may be regular. Myocyte hypertrophy, fibroses, scars, myocardial inflammation and viral genomes may be present. Amyloidosis and storage diseases have to be excluded.

ARVD/C:

Due to the main localization of the disease process, there are often no specific histological or immunohistochemical features and endomyocardial biopsy specimens may be regular. Myocyte

hypertrophy or atrophy, fibrosis, scars, myocardial inflammation and viral genomes may be present. A reduced expression of gap junction proteins (immunohistochemistry) may indicate ARVD. In the advanced stage of the disease, fibro-fatty degeneration of myocardial tissue proves ARVD.

Genetic/hereditary:

Genetic testing for specific gene defects/SNPs. In addition, histology, immunohistochemistry and molecular biology as defined above.

See references nr. 46-51

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7.3 NIH STROKE SCALE

Erläuterungen zur neurologischen Befunderhebung nach NIHSS

1a	Bewußtseinslage (Vigilanz)	(0) **Wach**, unmittelbar antwortend. (1) **Benommen**, aber durch geringe Stimulation zum Befolgen von Aufforderungen, Antworten oder Reaktionen zu bewegen. (2) **Somnolent**, bedarf wiederholter Stimulation um aufmerksam zu sein, oder ist soporös und bedarf starker oder schmerzhafter Stimulation zum Erzielen von Bewegungen. (3) **Koma**, antwortet nur mit motorischen oder vegetativen Reflexen oder reagiert gar nicht, ist schlaff und ohne Reflexe. *Anmerkung: bei Koma erhält Skala 7 (Extremitätenataxie) 0 Pkte.*
1b	Orientierung	**Frage nach Monat und Alter** (0) beide Fragen richtig beantwortet. (1) eine Frage richtig beantwortet. (2) keine Frage richtig beantwortet.
1c	Befolgung von Aufforderungen	**Aufforderung die Augen und die nicht paretische Hand zu öffnen und zu schließen** (0) beide Aufforderung richtig befolgt. (1) eine Aufforderung richtig befolgt. (2) keine Aufforderung richtig befolgt.
2	Blick-bewegungen (Oculomotorik)	(0) Normal. (1) Partielle Blickparese = wenn die Blickrichtung von einem oder bd. Augen abnormal ist, jedoch keine forcierte Blickdeviation oder komplette Blickparese besteht (e. g. Augenmuskelparese). *Auch bei unzureichender Kooperation 1 Pkt.* (2) Forcierte Blickdeviation oder komplette Blickparese, die durch Ausführen des oculocephalen Reflexes nicht überwunden werden kann.
3	Gesichtsfeld	(0) keine Einschränkung. (1) partielle Hemianopsie. (2) komplette Hemianopsie. (3) bilaterale Hemianopsie (Blindheit oder corticale Blindheit). *Anmerkung: Bei fehlender Beurteilbarkeit 0 Pkte.*
4	Facialisparese	(0) normal. (1) gering (abgeflachte Nasolabialfalte, Asymmetrie beim Lächeln). (2) partiell (vollständige oder fast vollständige Parese des unteren Gesichts). (3) vollständig auf einer oder bd. Seiten (fehlende Bewegungen unterer und oberer Teil des Gesichts).
5	Motorik Arme getrennt für links und rechts z. B. bei Tetraparese	(0) kein Absinken (der Arm wird über 10 Sekunden in der 90°/45° Position gehalten) (1) Absinken (der Arm wird zunächst bei 90°/45° gehalten, sinkt aber im Verlauf von 10 Sek. ab. (2) Anheben gegen Schwerkraft möglich (der Arm kann die 90°/45° Position nicht erreichen oder halten, sinkt auf die Liegefläche ab, kann aber gegen Schwerkraft angehoben werden) (3) Kein (aktives) Anheben gegen Schwerkraft, der Arm fällt nach passivem Anheben sofort auf die Liegefläche. (4) Keine Bewegung. *Anmerkung: bei Amputation oder Gelenkversteif. 0 Pkte; bei Plegie erhält Skala 7 (Extremitätenataxie) 0 Pkte.*
6	Motorik Beine getrennt für links und rechts z. B. bei Tetraparese	(0) Kein Absinken (das Bein bleibt über 5 Sekunden in der 30° Position). (1) Absinken (das Bein sinkt am Ende der 5 Sekundenperiode, berührt aber die Liegefläche nicht). (2) Aktive Bewegung gegen die Schwerkraft (das Bein sinkt binnen 5 Sek. auf die Liegefläche ab, kann aber gegen die Schwerkraft gehoben werden). (3) Kein (aktives) Anheben gegen die Schwerkraft, das Bein fällt nach passivem Anheben sofort auf die Liegefläche. (4) Keine Bewegung. *Anmerkung: bei Amputation oder Gelenkversteif. 0 Pkte; bei Plegie erhält Skala 7 (Extremitätenataxie) 0 Pkte.*
7	Extremitäten-ataxie	(0) fehlend. (1) in einer Extremität vorhanden. (2) in zwei Extremitäten vorhanden. *Anmerkung: wird bei Verständigungsschwierigkeiten oder Plegie als fehlend (0 Pkte.) gewertet. wird bei Angabe von Koma (s. Skala 1a) als fehlend (0 Pkte.) gewertet.*
8	Sensibilität	(0) Normal; kein Sensibilitätsverlust. (1) Leichter bis mittelschwerer Sensibilitätsverlust; Patient empfindet Nadelstiche auf der betroffenen Seite als stumpf, oder er nimmt diese nur als Berührung wahr. (2) Schwerer bis vollständiger Sensibilitätsverlust; Patient nimmt die Berührung von Gesicht, Arm und Bein nicht wahr.
9	Sprache	(0) normal; keine Aphasie. (1) Leichte bis mittelschwere Aphasie; deutliche Einschränkung der Wortflüssigkeit oder des Sprachverständnisses, keine relevante Einschränkung von Umfang oder Art des Ausdruckes. Die Einschränkung des Sprachvermögens und/oder des Sprachverständnisses macht die Unterhaltung schwierig bis unmöglich. (2) Schwere Aphasie; die Kommunikation findet über fragmentierte Ausdrucksformen statt. Der Untersucher muss das Gesagte in großem Umfang interpretieren, nachfragen oder erraten. Der Untersucher trägt im wesentlichen die Kommunikation. (3) Stumm, globale Aphasie; Sprachproduktion oder Sprachverständnis nicht verwertbar (auch bei Koma).
10	Dysarthrie	(0) Normal. (1) Leicht bis mittelschwer; der Patient spricht zumindest einige Worte verwaschen und kann nur mit Schwierigkeiten verstanden werden. (2) Schwer, anarthrisch; die verwaschene Sprache des Patienten ist unverständlich und beruht nicht auf einer Aphasie. *Anmerkung: Bei Intubation o. ä. 0 Punkte*
11	Neglect	(0) Keine Abnormalität. (1) Visuelle, taktile, auditive oder personenbezogene Unaufmerksamkeit oder Auslöschung bei Überprüfung von gleichzeitiger bilateraler Stimulation in einer der sensiblen Qualitäten. (2) Schwere halbseitige Unaufmerksamkeit. Kein Erkennen der eigenen Hand oder Orientierung nur zu einer Seite des Raumes. *Anmerkung: bei fehlender Beurteilbarkeit 0 Punkte*