



Guidelines on autopsy practice: Sudden death with likely cardiac pathology

March 2022

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Unique document number	G145
Document name	Guidelines on autopsy practice: Sudden death with likely cardiac pathology
Version number	3
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Date active	March 2022 (to be implemented within 3 months)
Date for review	March 2027
Comments	This document replaces earlier editions and is part of the 'Guidelines on autopsy practice' series. In accordance with the College's pre-publications policy, this document was on the Royal College of Pathologists' website for consultation from 5 January to 2 February 2022. Responses and authors' comments are available to view on publication of the final document. All other comments regarding this document should be sent to the College's non-forensic autopsy pathology lead, via clinicaleffectiveness@rcpath.org . Dr Brian Rous Clinical Lead for Guideline Review

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Registered charity in England and Wales, no. 261035

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For full details on our accreditation visit: www.nice.org.uk/accreditation.

Foreword

The autopsy guidelines published by the Royal College of Pathologists (RCPATH) are guidelines that enable pathologists to deal with non-forensic consent and coroner's post-mortem examinations in a consistent manner and to a high standard. The guidelines are systematically developed statements to assist the decisions of practitioners and are based on the best available evidence at the time the document was prepared. Given that much autopsy is single observer and one-time only in reality, it has to be recognised that there is no reviewable standard that is mandated beyond that of the RCPATH Part 2 examination or the Certificate of Higher Autopsy Training (CHAT). Nevertheless, much of this can be reviewed against ante-mortem imaging and other data. The increased use of digital photography and post-mortem computerised tomography (PMCT) has further assisted matters. This guideline has been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen type and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a specimen in a way that maximises benefit to pathologists, coroners and the deceased's family. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The medicolegal risk of departing from the guidelines should be assessed by the autopsy pathologist; just as adherence to the guidelines may not constitute defence against a claim of negligence, so a decision to deviate from them should not necessarily be deemed negligent. In all cases, clinical judgement should be used to tailor the post mortem to the needs of that specific case and the questions it raises.

There is a general requirement from the General Medical Council (GMC) to have continuing professional development in all practice areas and this will naturally encompass autopsy practice. Those wishing to develop expertise in or specialise in cardiac pathology are encouraged to seek appropriate educational opportunities and participate in the UK Cardiac Pathology Network external quality assessment scheme.

These guidelines themselves constitute the tools for implementation and dissemination of good practice.

The following stakeholders were contacted to consult on this document:

- the Human Tissue Authority and its Histopathology Working Group, which includes representatives from the Association of Anatomical Pathology Technology, Institute of Biomedical Science, the Coroners' Society of England and Wales, the Home Office Forensic Science Regulation Unit and Forensic Pathology Unit, and the British Medical Association
- the UK Cardiac Pathology Network
- the Coroners' Society of England and Wales.

The information used to develop this autopsy guideline was obtained by undertaking a systematic search of PubMed with ongoing review of cardiovascular literature including specialist cardiovascular journals. Previous versions of this guideline were also used to inform this update. Key terms searched included sudden death, heart, autopsy, cardiomyopathy, channelopathies and ischaemic heart disease, and dates searched were between January 2016 and December 2020. In addition, conference proceedings were analysed from the European Society of Pathology (ESP), the Society of Cardiovascular Pathology (SCVP) and the Association for European Cardiovascular Pathology (AECVP). Published evidence was evaluated using modified SIGN guidance (see Appendix A). Consensus of evidence in the guideline was achieved by expert review. Gaps in the evidence were identified by College members via feedback received during consultation.

No major organisational changes or cost implications have been identified that would hinder the implementation of this guideline.

A formal revision cycle for all guidelines takes place on a five-yearly cycle. The College will ask the authors of the guideline to consider whether the guideline needs to be revised. A full consultation process will be undertaken if major revisions are required. If minor revisions or changes are required, a short note of the proposed changes will be placed on the College website for two weeks for members' attention. If members do not object to the changes, the changes will be incorporated into the guideline and the full revised version (incorporating the changes) will replace the existing version on the College website.

The guideline was reviewed by the Clinical Effectiveness team, Death Investigation Committee and the Lay Network, prior to being placed on the College website for consultation with the membership from 5 January to 2 February 2022. All comments received from the membership were addressed by the authors to the satisfaction of the Clinical Lead for Guideline Review.

This guideline was developed without external funding to the writing group. The College requires the authors of guidelines to provide a list of potential conflicts of interest; this is monitored by the Clinical Effectiveness team and is available on request. The authors of this document have declared that there are no conflicts of interest.

1 Introduction

This document was created to address the needs of autopsy pathologists dealing with deaths due to cardiac disease. It suggests technical approaches and investigations that should prevent criticism of case analysis in a medicolegal environment. It should also serve to protect the needs of the living (i.e. surviving siblings and relatives with genetic conditions), as well as society in general. The pathologist will work closely with the local coroner (fiscal, or other medicolegal authority) and their officers since organ and tissue retention and permissions are unique to different cases and this documentary guidance should be useful for all such cases. The document is designed to be a focused bench-top guide with step-by-step examination suggestions.

The levels of evidence reflect published experience as summarised in the first two references. In some areas, this knowledge has been tested in legal settings and is cited as level D (see Appendix A), whereas most is given as good pathology practice.

1.1 Target users of this guideline

The target primary users of this guideline are established consultants performing medicolegal and consented autopsies. The recommendations will also be of value to trainees, particularly those approaching the CHAT examination and the FRCPath Part 2 in forensic pathology. In addition, these recommendations are of use in other types of specialist post-mortem examination (e.g. forensic post mortems) where the possibility of a cardiac cause of death is being considered.

2 The role of the autopsy

- To establish whether death is related to cardiac disease or another process.
- To establish the nature of the cardiac disease, if present.
- To consider whether the cardiac disease identified is related to systemic disease.
- To consider whether any cardiac disease is likely to be inherited or may be present in other relatives.
- To consider whether the cardiac disease could have been treated.
- To consider whether the cardiac disease is related to illicit activity (e.g. drug taking).

3 Other (not primarily cardiac) pathology to be considered at the autopsy

Many cases of apparent sudden 'cardiac' death have no relevance to myocardial disorders. Indeed, fatal non-cardiac pathology (with cardiac-like symptoms) may be often encountered:

- pulmonary embolism
- pneumonia
- pancreatitis
- peptic ulceration/peritonitis
- aortic aneurysm dissection/rupture
- cerebral pathology (tumours, intracerebral haemorrhage, trauma, etc.).

Deaths occurring suddenly in epilepsy (SUDEP) need to exclude co-existent cardiac disease.

Toxicology analysis may be highly relevant in the setting of any sudden unexpected death. The co-existence of illicit and/or therapeutic and prescribed drugs should be excluded. Cardiac and non-cardiac drugs should be considered as even standard non-cardiac medications may have a bearing on cardiac electrical and contraction function.

Alcohol may be associated with sudden death, often as a consequence of inebriation. One should also be aware of alcoholic cardiomyopathy/sudden death in association with alcohol misuse (SUDAM) and other cardiac functional abnormalities. Alcohol and drug interactions must also be considered.

4 Causes of sudden death involving cardiac disease

Coronary artery disease/ischaemic heart disease

- Atheroma.
- Coronary artery anomaly.
- Kawasaki disease (paediatric).
- Vasculitis/aortitis.
- Myocardial bridging (meeting appropriate criteria, ideally with evidence of previous ischaemia).
- Coronary artery dissection.
- Embolism into coronary arteries.
- Coronary artery vasculopathy (e.g. fibromuscular dysplasia of the coronary arteries, focal segmental mediolytic arteriopathy).
- Regional coronary artery spasm (with evidence of previous ischaemia).

Valve disease

- Aortic stenosis (senile/bicuspid).
- Mitral valve prolapse.
- Infective endocarditis (native valves and prostheses).
- Rheumatic valve disease.

- Tricuspid and pulmonary valve disease is less common, but mostly seen in the setting of congenital heart disease often with other structural lesions.

Myocardial disease

- Myocarditis (lymphocytic, eosinophilic, neutrophilic, giant cell, sarcoid/granulomatous).
- Cardiomyopathies (hypertrophic cardiomyopathy [HCM], dilated cardiomyopathy [DCM], arrhythmogenic cardiomyopathy [ACM] or restrictive cardiomyopathy [RCM]).
- Hypertensive heart disease seen with left ventricle hypertrophy.
- Obesity-associated cardiomyopathy, often with hypertrophied myocardium and/or dilatation.
- Diabetic cardiomyopathy.
- Idiopathic myocardial fibrosis.
- Cardiac amyloid.
- Storage disorders (e.g. Anderson-Fabry disease, but many other types exist).
- Connective tissue disorders (rheumatoid arthritis, systemic lupus erythematosus), sickle cell (HbSS) and endocrine disorders (e.g. hypothyroid and hyperthyroid states).

Congenital heart disease (± surgically corrected)

This is also known as grown-up congenital heart disease.

Cardiac tumour

Most tumours involving the heart are metastatic tumours from the lung, breast or gastrointestinal tract. Rarely tumours grow up the inferior vena cava, such as renal cell carcinomas and uterine leiomyomas, potentially extending into the right atrium or causing tumour emboli into the lungs. Most primary cardiac tumours are myxomas. There are a small number of other benign lesions and rarely primary malignant lesions of the myocardium or large vessels (sarcoma).

Structural abnormalities of the conduction system

- Absence of part of the atrioventricular (AV) node.
- Damage to the AV node and His bundle with fibrosis, including ablation therapy.
- Inflammation (e.g. sarcoid).
- Cystic tumour of the AV node.
- Wolff-Parkinson-White syndrome and other aberrant pathways.

Note: it is difficult to serial section the whole conduction system, and diagnoses such as Wolff-Parkinson-White syndrome are commonly made clinically and electrophysiologically. Nonetheless, targeted blocks of areas of interest may be pertinent to consider fibrous replacement of the AV node and bundle of His.

Drug toxicity

Cocaine, amphetamines, ecstasy, new psychoactive substances, solvents, psychiatric medications (antidepressants/antipsychotics) and cardiac drugs are the drugs most likely to be implicated in cardiac-related deaths, but others may be relevant.

[Level of evidence – GPP.]

No morphological abnormalities (sudden arrhythmic death syndrome)

- Channelopathies.
- Metabolic disease.
- Takotsubo cardiomyopathy (with appropriate ante-mortem imaging).
- Commotio cordis (with relevant specific chest trauma documentation).

Pregnancy

Sudden cardiac death in pregnancy and the early post-natal period remains a rare but recognised process. Indeed, one should always look for common cardiac pathologies such as coronary disease (e.g. atheroma and dissection), hypertension, valve disease (unmasked by the extra-cardiac demands of pregnancy) as well as specific pathologies (post-partum cardiomyopathy) and sudden arrhythmic death syndrome (SADS). This list is not exhaustive and all-encompassing, but it highlights the common lesions to be considered.

5 Specific health and safety aspects

The deceased may have pacemaker, cardiac resynchronisation pacemaker or defibrillator device, or loop recorder in situ. Some cardiac/vascular devices may be composed of metal and could pose a hazard with sharp edges when cut for extraction.¹ Patients with cardiac pacemakers should have these interrogated by cardiologists prior to autopsy as they may provide information on terminal cardiac arrhythmias and cause of death. It is stressed that some pacemakers (resynchronisation and defibrillator devices) require deactivation prior to body examination and all standard/resynchronisation pacemakers should also be removed prior to cremation because of the risk of explosion when heated. There is a separate document on medical devices found at autopsy, which will be published by RCPATH in due course.

[Level of evidence – GPP.]

6 Relevant information required before the autopsy commences

It is recognised that not all of the data below is always available prior to the examination. The pathologist needs to start only when they are satisfied there is sufficient data.

- Circumstances including time and date of death.
- Witness statements.
- Previous medical history.
- Medical therapy regimen (current and prior).
- Previous surgical operations and other interventions.
- Alcohol usage ± illicit drug use.
- Family history.
- Electrocardiogram (ECG) results, enzyme results and other pathological data.
- Serum lipid profiles and other biochemical tests.

[Level of evidence D – the evidence has been taken from reviews of various texts/case reports and other presented cases, in medical and legal settings.]

7 The autopsy procedure

- A standard autopsy is required but with particular emphasis on the cardiac and vascular tissues.
- Body mass is important to cross compare with the heart weight.
- Examination of the cranial, lung, liver and kidney tissues must be done to give a balanced case analysis.
- Staged dissection is recommended with consideration of any devices and their site, orientation and functionality. If necessary, the whole device should be retained for subsequent analysis. Care should be taken to deactivate any device prior to commencing the autopsy if it poses any risk to those conducting the autopsy (see *Guidance for pathologists conducting post-mortem examinations on individuals with implanted electronic medical devices*).²
- Regular photography as the examination progresses is recommended.
- The position of vascular access lines, tubes for ventilation, ECG pads, defibrillator units, etc., should be recorded.

[Level of evidence – GPP.]

8 The standard examination of the heart

The heart should be dissected in line with standard text guidelines,^{1,3} but the standard process is summarised below.

- Check pericardium for adhesion, effusions, exudates and blood accumulation.
- Transverse sections of the aorta, venae cavae and pulmonary veins to release the heart, making sure that the transection is 1 cm above the right superior vena cava/atrium interface to preserve the sinoatrial node.
- Internal palpation of the pulmonary artery root to check for pulmonary emboli.
- Check the two coronary artery origins and vessel distribution on the heart surface to exclude congenital anomalies.
- Examine any vein/internal mammary artery grafts. Check these bypass grafts and their patency. Possible retention of graft/native vessel interface/anastomosis for histology.
- Examine any devices applied.
- Transverse section of the coronary arteries sequentially (3–5 mm intervals) to exclude significant lumen obstruction by atheroma or other disease process. Examine left coronary including left main stem, left anterior descending and circumflex with obtuse marginal branches. Examine the right coronary including right marginal branch and the posterior descending coronary artery. The evaluation of any stenosis is accepted as not absolute, but most pathologists are competent at assessing the grade of narrowing in the proximal coronary arteries. Absolute definition of the sampled artery lumen may require histology.
- Arteries with stents can be opened longitudinally with sharp scissors, removed and checked for thrombus macroscopically. An alternative would be to use a scalpel to cut down onto the stented vessel to inspect the stent lumen. Thrombus filling the lumen can be removed for standard histology. Long-standing stents will be endothelialised and impossible to remove from the vessel wall intact. Radiology may occasionally be of use in stented areas and compared with ante-mortem imaging.

- Transverse section across the ventricles up to the midsection of the ventricular tissues. This preserves the chordae and valvular tissues.
- Consider the chamber lumens and wall thickness. If felt necessary, take measurements at mid-ventricular level or 1 cm below valves in right and left ventricular outflow tracts, and record these in the report. Photography may be helpful.
- Opening the rest of the heart should be generally in the style of the ‘flow of blood’.
- The posterior right atrium and posterior aspect of the right ventricle are opened, showing the atrial/ventricular junction. The foramen ovale should be confirmed as closed, or probe patent. Check the intact tricuspid valve before cutting from the right atrium to ventricle on the posterior aspect.
- The anterior right ventricle is opened into the pulmonary outflow tract and across the pulmonary valve.
- The left atrium is opened across the four veins. Check the intact mitral valve for prolapse up into the left atrium. Then a cut is made down the lateral wall or the back of the left atrium and down across the back of the left ventricle close to the septum to examine the mitral valve and atrial/ventricular junction.
- Check up into the left ventricular outflow tract to see intact aortic leaflets or else view via cut aorta from above. The anterior aspect of the left ventricle is opened alongside the left anterior descending artery and across the aortic valve, passing behind the left main stem in front of the left atrial appendage. This allows examination of the aortic valve and coronary openings. Another method is cutting through the anterior leaflet of the mitral valve once inspected up into the ascending aorta to open out the outflow tract and inspect the coronary artery ostia.
- Cardiac weight can now be assessed, once all blood/clot is removed. This should be compared against the body mass and/or standard cardiac weight tables.
- Any zones of fresh or previous infarction should be identified and quantitated.
- Fat replacement and scarring should be looked for carefully in the myocardium of both the right and left ventricle.
- Infiltrates are more difficult to identify, but general thickening of the myocardium and irregular stiffness of the tissues may be a clue to infiltrative diseases.

[Level of evidence – GPP.]

9 Histological examination

Clinical judgement must be used to assess the need for histology in each individual case, with some cases with an overt cause of death potentially not needing samples. When the cause of death is not clear but is felt likely to lie within the cardiovascular system, there should be a very low threshold for taking the relevant histological samples. Any sampling must be within the limits of consent in the case of a consented autopsy or within the limits of the relevant medicolegal legislation and guidelines, if the case is of a medicolegal nature. When the cause of death is felt to lie within the heart, but in which no obvious lesion is identified, sampling for histology is essential as a normal-looking heart can have myocarditis, storage disease or cardiomyopathy microscopically. In such cases, the extent of sampling will be governed by the clinical judgement of the pathologist performing the autopsy. However, where possible as a minimum, it is recommended to take mapped blocks of anterior, lateral and posterior right and left ventricle and septum from a representative mid-ventricular transverse slice and right ventricular outflow tract. More intensive sampling would include part/all the coronaries, the tissues from the sinoatrial node and AV node, and a complete mid-ventricular slice.

Alternatively, retention of the whole heart and sending it intact to a specialist centre for expert opinion should be considered.

The role of histology in cardiac tissue evaluation is important, and blocks should ideally be taken to illustrate any cardiac disease – such as one block from an infarcted area and one block from the thrombosis within a vessel (can be useful to detect dissection especially in younger people) or maximal area of narrowing with decalcification if necessary.

In all cases where an inherited cardiac condition is being considered as the cause of death from macroscopic examination, obtaining histology for confirmation is essential to support and strengthen the diagnosis. If there is no apparent focal lesion, multiple blocks should be taken across the right ventricle and left ventricle/septum, or potentially large blocks should be taken to encompass the entire ventricular ring/septal tissues.

Samples of the right and left atria are generally not needed, unless there is a focal lesion.

Additional histochemical stains may be of use to assist general stains. A connective tissue stain (elastic van Gieson or Masson's trichrome) is advisable. Congo/Sirius red (for amyloid), Perl's Prussian blue (for iron), PAS/ABPAS (for storage disorders) and immunohistochemistry for CD3, CD20, CD68, etc. (for myocarditis) should be performed as required. C4d staining in transplant cases and C9 immunohistology may assist in cases of ischaemia. Rarely, a sample may be reserved for possible electron microscopy.

In cases where the cause of death is felt to be cardiac but in which no obvious abnormality is identified, it may be prudent to also sample background lung as well as kidney, liver and/or other relevant tissues as determined by the observed pathology.

In all cases, the histological sampling required must be guided by the clinical judgement of the pathologist conducting the case and the specific requirements of the case.

[Level of evidence – GPP.]

10 Other samples that may be relevant

- If illicit drug use is suspected, peripheral blood, vitreous and urine should be sent for analysis.⁴
- In all negative autopsies, toxicological samples should be taken.
- If acute anaphylaxis is suspected, peripheral blood should be sent for mast cell tryptase analysis (if possible, spun peripheral blood serum should be taken but it is recognised that this may not be possible in many mortuaries).⁵
- If myocarditis is suspected, a piece of fresh heart tissue should be retained for microbiological and viral studies where possible.
- If a potentially inheritable disorder of the heart or thoracic aortic dissection in a person under the age of 40 is suspected, fresh blood and/or a 2 cm cube of fresh spleen should be reserved for future genetic testing (molecular autopsy).⁶ Clinical judgement for sampling in such cases can be exercised by the pathologist in those over the age of 40. The authority/consent for this retention must, however, be ensured by the pathologist conducting the post mortem – be that through obtaining consent from someone in a suitable qualifying relationship to the deceased or through confirmation that such retention lies within the jurisdiction of the medicolegal authority responsible for that case (as coronial practice varies widely with respect to this issue). Most coroners' officers are familiar with the procedures for tissue retention and can obtain consent from the next of kin or person who is appointed to give legal consent when the pathologists deems this to be necessary in an autopsy. The fiscal/coroner's officer/pathologist must inform the

family when this sample is taken as well as other tissue samples for histology for medicolegal and consented cases respectively. If possible, the sample should be frozen or put directly into RNAase later, pending onward referral for genetic testing. Failing that, the sample should be refrigerated and sent at the earliest opportunity, as fast as possible, to the genetic centre where longer term storage can be addressed. Genetic testing is now provided on all autopsy samples within the NHS Genomic Medical Service Alliance in consultation with the specialist who can screen the family for genetic causes in England.

- In paediatric cases, the possibility of inborn errors of metabolism should be considered and appropriate samples (guided by clinicians and the paediatric clinical biochemist) should be reserved.

[Level of evidence – GPP.]

11 Organ retention

Ideally, the heart should be retained until all investigations are complete, whether by the primary or specialist cardiac pathologist. However, one has to be mindful of family, religious and cultural feelings on this matter. The benefit of having digital images of progressive dissection of cardiac tissues and then localised or targeted sampling is important. This can often remove the need for whole organ retention. The heart can be returned rapidly to the body once sampling is performed by the pathologist, so a delayed funeral is avoided.

In potential cases of inherited cardiac disease, it is important to advise the family to retain tissue blocks and slides. While slide scanning is increasingly used and a useful medium, the value of retaining some tissue in a paraffin-based format cannot be underestimated with evolving antibodies and other molecular tests.

In cases with medicolegal implications (usually those with forensic potential), cardiac tissue should ideally be retained until the police, court or coroner/fiscal completes their investigations.

[Level of evidence – GPP.]

12 Imaging and the cardiac autopsy

Post-mortem imaging is increasingly used in cases of sudden death. Its use varies across the UK and its role in cardiovascular pathology is still evolving. At present, PMCT with/without angiography appears to be the mainstay for investigations. This is covered in the RCPATH's *Guidelines for post-mortem cross-sectional imaging in adults for non-forensic deaths*.⁷ Imaging may provide information on valve calcification, myocardial infarction, aortic dissection/aneurysm rupture, but it is not absolute. Normal hearts and likely cardiomyopathies ideally should have open examination, histology and other tests for diagnosis.

[Level of evidence – level D.]

13 Specific categorisation of sudden cardiac deaths

All causes of sudden cardiac death have to be correlated with the available clinical data and autopsy pathology findings. Simply finding some atheroma or microscopic small foci of scarring does not necessarily make this the cause of death.

Maternal deaths are rare and cardiac causes are now predominating, instead of direct obstetric complications or infection.

For cases of ischaemic/atheroma-related deaths, the coronary artery tissues should only be regarded as being of significance to the cause of death where there is 70% or more stenosis (e.g. lumen less than 1 mm), where one can show adherent/occluding thrombus or where there is ante-mortem evidence of high-grade occlusion by means of imaging criteria. This causes fatal cardiac dysrhythmia, and complete occlusion by thrombus of such vessels can be the trigger factor, which may have disappeared prior to post mortem.

Lesser degrees of atheroma (less than 70% stenosis) can also have the same outcome, but this must be tested against absence of other pathology before deciding that this was the cause of death (on the balance of probability). It should be remembered that lower grade atheroma may be complicated by acute plaque rupture/thrombosis, which raises the degree of luminal obstruction dramatically and suddenly. This is often the cause of acute or zonal myocardial infarction. The finding of an acute myocardial infarct should point to the risk of cardiac dysrhythmia, culminating in ventricular fibrillation and cardiac arrest.

Ischaemic heart disease of both acute and chronic patterns of myocardial scarring/damage is associated with cardiac dysrhythmias and death.

Acute and chronic myocardial infarction is also associated with 'pump failure'. Here, the infarcted heart fails to maintain adequate cardiac output, with secondary consequences on the lungs (pulmonary oedema and pleural effusions), kidneys (tubular necrosis) and liver (centrilobular necrosis).

Valvular heart disease is less common, and often under-appreciated, as a cause of sudden cardiac death. It is important to assess the severity of any valvular disease, and fully measure the ventricular chamber diameters and wall thickness.

It may be necessary to take representative histology of the lungs, especially in congenital heart disease and when there is right ventricular hypertrophy pointing to pulmonary hypertension.

Myocarditis is usually multifocal within the myocardium, and the myocardial sampling as recommended will usually detect multiple inflammatory infiltrates. Fresh myocardium and blood may be useful for virology and serology in consultation with the local microbiology laboratory. Abnormal infiltrates, such as amyloid, should be sought.

Cardiac tumours are rarely encountered and their significance should be balanced against the ante-mortem history and other autopsy findings. Look for emboli into the coronary circulation, particularly with myxomas and fibroelastomas.

Cardiomyopathies deserve special mention. These include DCM (multiple causes being recognised), HCM, ACM and other degenerative cardiomyopathies (mitochondrial, muscular dystrophy, etc.). These cardiomyopathies are usually associated with progressive cardiac failure as well as a risk of cardiac dysrhythmic death.

Cardiac hypertrophy, without overt genetic/structural aetiology, may be recognised as a cause of sudden death, but it requires exclusion of hypertension, genetic cardiomyopathic disease, infiltrates and valvular disease. However, to invoke cardiac hypertrophy (not otherwise specified) requires a cardiac mass in excess of 30% above expected and no other drivers for the hypertrophy. Cardiac hypertrophy can be linked to obesity and diabetes in absence of coronary artery disease.

Finding a sudden death where there is no cardiac anomaly could point towards SADS. Criteria to explore this potential cause of death include negative general autopsy findings, both macroscopic and histological, along with negative toxicology and a morphologically normal heart. In such cases, it is strongly recommended that the heart is retained in its entirety and

either sent for expert cardiac opinion or examined histologically in detail locally in an attempt to elucidate any underlying cause.

Note: it is essential that a 2 cm cube of fresh spleen is be retained, as described above.

[Level of evidence – GPP.]

14 Clinicopathological correlation

It may be valuable to discuss the case with clinical colleagues as part of a multidisciplinary team, especially when there is the possibility of a genetic cause or there has been a diagnosis made prior to death. Clinical liaison with the general practitioner and/or specialists in the hospital setting within an inherited cardiac condition service may assist with the case review, as well as potentially enhancing the understanding of relatives. This is advisable before the pathologist issues the final report.

The pathologist should be prepared to speak to relatives about pathological findings and explain them carefully and sensitively in layman language, whether it be in the court setting or in a more neutral environment.

Referral of close relatives (i.e. parents and siblings) to inherited heart disease clinics will be of benefit when a genetic cause is suspected, particularly with SADS and cardiomyopathies. The need for this should be highlighted in the post-mortem report so that those in receipt of this report can arrange follow up with the relatives. This may be through the general practitioner. The College believes that while it is the responsibility of the pathologist to highlight the fact that such follow up may be beneficial, it is not up to the pathologist or pathology department to arrange such follow up. Rather, it is the responsibility of the person in receipt of the post-mortem report, be that the lead clinician or the medicolegal authority.

Ideally, the words 'cardiac failure' should not appear as part of the cause of death formulation. While it is often of benefit to individual families to have it explained thus, it is better to define the cardiac pathology in its technical format. 'Acute cardiac failure due to myocardial infarction, due to coronary artery thrombosis' may be easier to follow for relatives. However, it is debatably less pathologically rigorous than the alternative: 'myocardial infarction, due to coronary thrombosis'.

[Level of evidence – D.]

15 Examples of cause of death opinions/statements

- 1a. Acute myocardial infarction
- 1b. Coronary artery thrombosis with atheroma

- 1a. High grade (i.e. 90%+) occlusive coronary atheroma (i.e. no infarction)

- 1a. Myocardial infarction
- 1b. Occlusive coronary atheroma

- 1a. Cardiomyopathy (note: specify the subtype, HCM, DCM, ACM or RCM)

- 1a. Aortic and mitral valve disease

- 1b. Rheumatic valvular disease

- 1a. Acute myocarditis

- 1b. Echovirus infection
- 1a. Sudden arrhythmic death syndrome (note: this will usually require a detailed discussion of the relevant possibilities and suggested investigations)
- 1a. Left ventricular hypertrophy (note: this will require usually a detailed discussion of the relevant possibilities and suggested investigations. It is likely that correlation against body mass and height data will be relevant, but one must be aware that a variety of social, racial and gender factors need to be considered)

Note: Modes of death, such as cardiac failure, cardiac arrest, arrhythmia or dysrhythmia, should not feature, as one should aim to delineate solely the pathology.

[Level of evidence – GPP.]

16 Criteria for audit

The following standards are suggested criteria that might be used in periodic reviews to ensure a post-mortem report for coronial autopsies conducted at an institution complies with the national recommendations provided by the 2006 NCEPOD study.⁸

- Supporting documentations:
 - standards: 95% of supporting documentation was available at the time of the autopsy
 - standards: 95% of autopsy reports documented are satisfactory, good or excellent.
- Reporting internal examination:
 - standards: 100% of autopsy reports must explain the description of internal appearance
 - standards: 100% of autopsy reports documented are satisfactory, good or excellent.
- Reporting external examination:
 - standards: 100% of autopsy reports must explain the description of external appearance
 - standards: 100% of autopsy reports documented are satisfactory, good or excellent.

A template for coronial autopsy audit can be found on the Royal College of Pathologists' website (www.rcpath.org/clinical-effectiveness/clinical-audit/clinical-audit-templates).

17 References

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Appendix A Summary table – explanation of levels of evidence

(modified from Palmer K *et al. BMJ* 2008;337:1832.)

Level of evidence	Nature of evidence
Level A	At least one high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Level B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in A.
Level C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high-quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in B.
Level D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group.

Appendix B AGREE II compliance monitoring sheet

The accredited guidelines of the Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of this guideline that indicate compliance with each of the AGREE II standards are indicated in the table below.

AGREE II standard	Section of guideline
Scope and purpose	
1. The overall objective(s) of the guideline is (are) specifically described	Foreword
2. The clinical question(s) covered by the guidelines is (are) specifically described	Foreword
3. The patients to whom the guideline is meant to apply are specifically described	Foreword
Stakeholder involvement	
4. The guideline development group includes individuals from all the relevant professional groups	Foreword
5. The patients' views and preferences have been sought	N/A
6. The target users of the guideline are clearly defined	1.1
7. The guideline has been piloted among target users	Foreword
Rigour of development	
8. Systematic methods were used to search for evidence	Foreword
9. The criteria for selecting the evidence are clearly described	Foreword
10. The methods used for formulating the recommendations are clearly described	Foreword
11. The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword
12. There is an explicit link between the recommendations and the supporting evidence	Throughout
13. The guideline has been externally reviewed by experts prior to its publication	Foreword
14. A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15. The recommendations are specific and unambiguous	2–15
16. The different options for management of the condition are clearly presented	Foreword
17. Key recommendations are easily identifiable	2–15
18. The guideline is supported with tools for application	Throughout
Applicability	
19. The potential organisational barriers in applying the recommendations have been discussed	Foreword
20. The potential cost implications of applying the recommendations have been considered	Foreword
21. The guideline presents key review criteria for monitoring and/or audit purposes	16
Editorial independence	
22. The guideline is editorially independent from the funding body	Foreword
23. Conflicts of interest of guideline development members have been recorded	Foreword