MINOCA and Sudden Cardiac Death: a Clinical and Pathological Perspective

Giuseppe Ciliberti[1 *] MD, PhD; Gherardo Finocchiaro[2,3 *] MD, PhD; Michael Papadakis[4] MRCP, MD; Joseph David Westaby[5], CHAT, FRCPath; Sanjay Sharma[4] BSc, MRCP, MD; Mary N. Sheppard[5], BSc, MD, FRCPath, FRCPI

[1]Cardiology and Arrhythmology Clinic, Marche Polytechnic University, University Hospital "Ospedali Riuniti", Ancona, Italy; [2]Guy's and St Thomas' NHS foundation trust, London, United Kingdom; [3]King's College London, United Kingdom; [4]Cardiology Clinical Academic Group, Molecular and Clinical Sciences Research Institute, St George's, University of London, United Kingdom; [5]Cardiovascular Pathology Department, St George's, University of London, London, United Kingdom

*Equally contributed as first author

Correspondence to:
Professor Mary N. Sheppard, MB, BCH, BAO, BSc, MD, FRCPath,
Professor of Cardiac Pathology
Cardiology clinical and academic group
St. George's University of London
Cranmer Terrace, London. SW17 0RE. UK.
E-mail: msheppar@sgul.ac.uk

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Non-standard Abbreviations and Acronyms:

LV: Left Ventricle

MI: Myocardial Infarction

MINOCA: Myocardial Infarction with Non-Obstructed Coronary Arteries

NOA: Non-obstructive Atherosclerosis

RV: Right Ventricle

SCD: Sudden Cardiac Death

Myocardial infarction with non-obstructed coronary arteries (MINOCA) accounts for 1-10% of all causes of acute myocardial infarction (MI) and may be secondary to various specific aetiologies with implications for prognosis[1]. The aim of the study was to describe the clinical and pathological features of a cohort of decedents of sudden cardiac death (SCD) attributable to MINOCA at autopsy.

MINOCA was defined as evidence of acute MI and/or acute coronary thrombosis in the absence of epicardial coronary artery stenosis ≥50%[1,2]. The data that support the findings of this study are available from the corresponding author upon reasonable request.

We reviewed a database of 5325 consecutive cases of SCD referred to our specialist cardiac pathology center between 1994 and July 2017. SCD was defined as death from a cardiovascular cause within 12 hours of apparent well-being. Clinical information was obtained from referring coroners who were asked to complete a questionnaire inquiring about the demographic characteristics of the decedent, medical history, family history and circumstances of death. All cases underwent detailed autopsy evaluation of the heart, including histological analysis, by expert cardiac pathologists[3]. A minimum of 10 blocks of tissue were taken for histological analysis. The origin of each artery was identified and a probe with a diameter of 2mm inserted in the coronary ostia to assess the presence of stenosis. The vessels were then dissected and examined with transverse cuts each 2mm throughout their whole length.At least 10 sections (average 13) of myocardium were then taken and stained with haematoxylin and eosin as well as elastic Van Gieson stain.

Exclusion criteria included specific cardiac conditions as previously reported[4], including myocarditis and Tako-Tsubo cardiomyopathy, which were ruled-out by clinical records examination[3] and through histology[3,4] . Non-obstructive atherosclerosis (NOA) was defined

by the presence of atheroma in any coronary section resulting in coronary stenosis <50%. Ethical and research governance approval have been granted for this study (10/H0724/38). The next of kin consented to material retention for anonymized research in each case.

We identified 37 (0.7%) cases of MINOCA. The majority of decedents were male (n=23; 62%). Mean age at death was 34±16 years (range 13-96 years), and 6 individuals were <18 years of age (Figure 1). Cardiac symptoms were reported in 18 cases (49%): chest pain (n=12; 32%), dyspnoea (n =6; 16%), syncope (n=2; 5%) and palpitations (n=1; 3%). None of decedents had a pre-mortem diagnosis of ischemic cardiac disease. Death occurred at rest or during daily activities in 36 (97%) individuals, including 9 (24%) who died during sleep. According to the information available, 2 decedents were reported to be currently smokers, 1 was ex-smoker and 3 were reported as "never smoked".Drug use was reported in 10 (27%) including marijuana in 3 (8%), cocaine in 2 (5%), heroin in 2 (5%), methadone in 2 (5%), anabolic steroids in 2 (5%), amphetamine in 1 (3%) cases. Of the 10 cases, toxicology testing showed the presence of the same substance in 30% at non-toxic levels. The coronary dominance was right in 36, co-dominant in 1. NOA was found in 13 patients (35%). Coronary thrombosis was found in 9 out of 13 (69%) patients with NOA and the mechanism of thrombosis was plaque erosion in 7 (78%) and fissuring in 2 (22%). The MI age was 24-48 hours in 28 cases (76%) and 1-6 weeks in the rest of decedents. The MI histological changes were found at the level of the left ventricular (LV) anteroseptal wall in 14 (38%) individuals, the LV and right ventricular (RV) subendocardial wall in 9, the LV postero-basal wall in 6, the RV and LV diffusely in 5, the LV lateral wall in 2 cases; in 1 case the MI involved exclusively the right atrium leading to atrial wall rupture and subsequent cardiac tamponade. In a minority (n=9; 24%) LV fibrosis was detected in a myocardial territory that

was different from the one of the MI, with a subendocardial distribution in 3 cases and near transmural (75% of the myocardial wall) in 1.

Our study reports on the largest autopsy cohorts of individuals with SCD due to MINOCA in which the post-mortem was performed by an expert cardiac pathologist following a standardized protocol. Most deaths occurred at rest, although almost half of the decedents reported cardiac symptoms. Toxicology analysis was positive in one out of three victims with background of drug use, thus representing a possible aetiological mechanism for both MINOCA and SCD. Ischaemic damage had a diffuse or regional pattern with the anteroseptal wall most often involved. In a minority, replacement fibrosis with an ischemic pattern was identified in a territory that was different from the one of the acute MI, implying that subclinical MI may have occurred before SCD, representing a substrate for arrhythmias. Of interest, coronary thrombus was exclusively found among patients with NOA, whereas among patients with no macroscopic evidence of atherosclerotic plaque coronary spasm possibly played a role. Our study has some limitations. It is possible that we may have underestimated the proportion of individuals with MINOCA who presented with SCD as the first manifestation because local pathologists may not have referred decedents with an established pre-mortem diagnosis of MI to our center. However, our center receives a high volume of referrals (>500 SCD cases per year - mostly young decedents); furthermore, MI with normal coronary arteries is likely to be considered an uncertain finding by a non-expert cardiac pathologist and therefore referred to for our assessment. The lack of electrocardiogram in decedents of SCD is also a limitation. Moreover, although MINOCA was originally a pathological definition, to date it remains a clinical diagnosis and post-mortem pathological examination can confirm or exclude the presence of an anatomical

substrate of MI[5]. In conclusion, MINOCA is an uncommon cause of SCD which usually occurs in young individuals, often at rest or during daily activities and cardiac symptoms are reported in almost half of the cases. The high proportion of decedents reporting use of drugs and anabolic steroids underscores a possible mechanistic link with MINOCA and SCD especially in young individuals.

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Disclosures

Dr. Ciliberti has nothing to disclose.

Dr. Finocchiaro has nothing to disclose.

Dr. Papadakis has nothing to disclose.

Dr. Westaby has nothing to disclose.

Prof. Sharma has nothing to disclose.

Prof. Sheppard has nothing to disclose.

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Figure legend

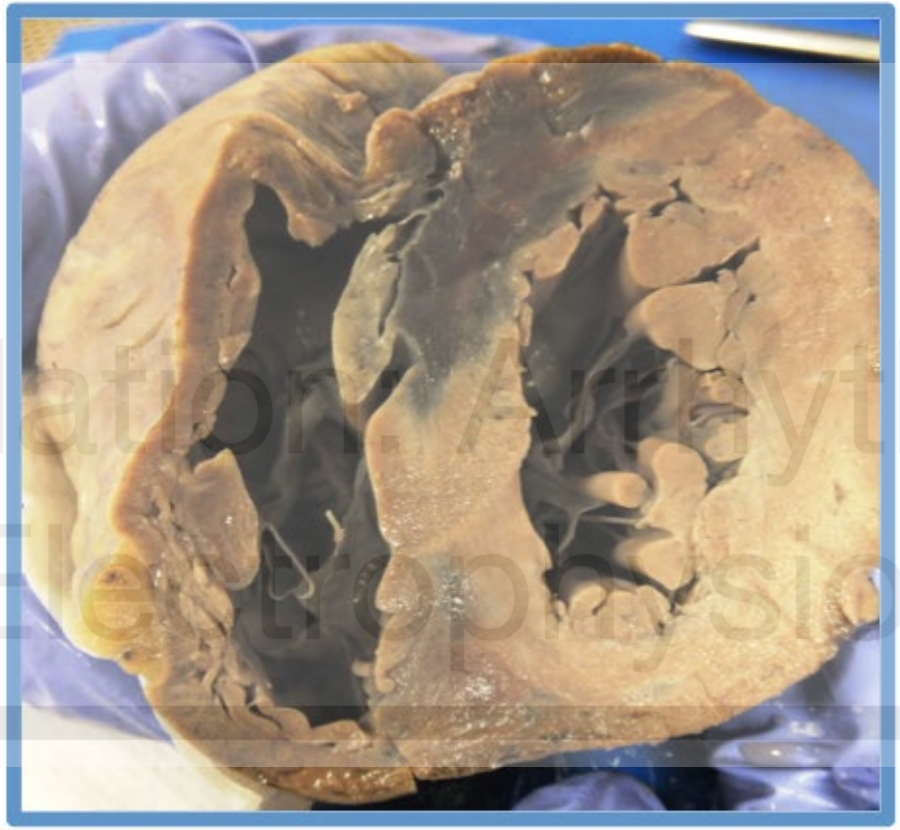
Figure 1. Sudden cardiac death in patients with MINOCA.

LV, left ventricle; MI, myocardial infarction; MINOCA, myocardial infarction with non-obstructed coronary arteries.

Non-obstructive atherosclerosis in 35%

Average age 34±16 years
16% <18 years old

MI age 24-48 hours in 76%



62% Males

Anteroseptal MI in 38 %

Cardiac symptoms in 49%

LV fibrosis in 24%

Drug use in 27%