

## The Silent Heart: Chronic Cardiac Disease in Post-Mortem Substance Overdose Cases

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**Received:** 15 Jan 2026; **Accepted:** 01 Mar 2026; **Published:** 15 Mar 2026

**Citation:** Dowling Geraldine M, Hartel Paul H. The Silent Heart: Chronic Cardiac Disease in Post-Mortem Substance Overdose Cases. American J Pathol Res. 2026; 5(2): 1-3.

### ABSTRACT

This study examined 15 post-mortem overdose cases (three females, 12 males; age range 28–78 years, mean 56). Chronic comorbidities included depression, seizure disorder, diabetes, and hypertension. Toxicology revealed lethal or toxic levels of multiple substances, predominantly opioids, antidepressants, ethanol, and benzodiazepines, with 13 cases involving poly-substance use. Gross cardiac findings included severe coronary artery disease, dilated cardiomyopathy, and left ventricular hypertrophy, while histology revealed ischemic changes, myocardial infarction, and heart failure. Chronic cardiac pathology was present in 73% of cases, despite only 20% showing conventional cardiovascular risk factors; in decedents under 60, 89% had cardiac pathology versus 33% with risk factors. Findings indicate that substance use, particularly polypharmacy, may contribute to silent cardiac disease, highlighting the need for cardiac screening in substance-using populations.

### Keywords

Cardiovascular Pathology, Drugs of Abuse, Overdose, Post Mortem.

### Introduction

The contribution of underlying cardiac disease to deaths following drug, alcohol, or toxic substance overdose remains incompletely characterised in post-mortem populations. In living overdose

patients, adverse cardiovascular events are well documented, with cohort data demonstrating that approximately 9–16% experience myocardial injury, dysrhythmia, shock, or cardiac arrest after overdose exposure [1,2]. However, translating these clinical observations to the forensic setting is challenging. Major causes of death related to substance use include overdose, cardiovascular disease, malignancy, and infection, with cardiovascular pathology encompassing coronary artery disease, arrhythmias,

and ischaemic events [2]. Determining whether cardiac disease represents a primary cause of death, a contributory factor, or an incidental finding at autopsy is a persistent diagnostic dilemma for pathologists [3].

Emerging post-mortem studies suggest that structural and histopathological cardiac abnormalities are common in drug-related deaths. In a large autopsy investigation, opioids, benzodiazepines, and alcohol were associated with more severe cardiovascular pathology, including atherosclerosis and myocardial inflammation [2]. Stimulant-related fatalities further demonstrate high rates of myocardial fibrosis, inflammatory infiltrates, and degenerative change, with cardiovascular lesions reported in up to 68% of methamphetamine poisoning deaths [4]. Additionally, toxicological analyses in sudden cardiac death cohorts reveal frequent exposure to alcohol and other cardiotoxic substances at the time of death [5].

Collectively, these findings highlight the complex interplay between substance toxicity and pre-existing cardiovascular disease, underscoring the need to clarify the prevalence and pathological significance of cardiac findings in post-mortem overdose cases.

## Methods

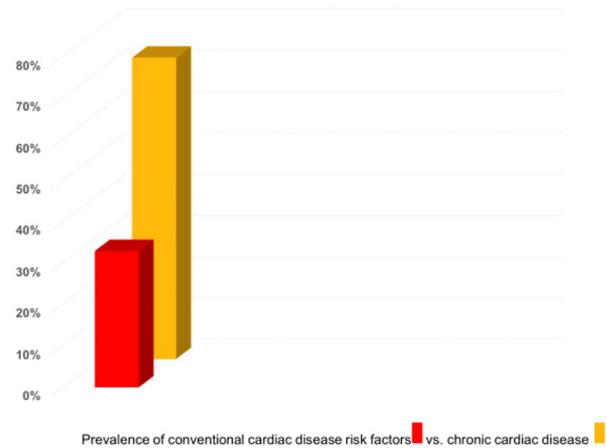
Following CoPath electronic archive audit of post-mortem cases from 2018-2022 using 'overdose,' anonymized post-mortem reports from all 15 cases were included. Post mortems were performed by specialist registered consultant pathologists.

Clinical data, gross and histopathologic cardiac findings (hematoxylin and eosin stained slides) and State Laboratory toxicology results were reviewed. Prevalence of chronic cardiac disease pathology and conventional cardiac risk factors (such as hypertension, diabetes, smoking) were tabulated. Patients aged 60 years and older were excluded in second analysis to eliminate age-related cardiac disease risk.

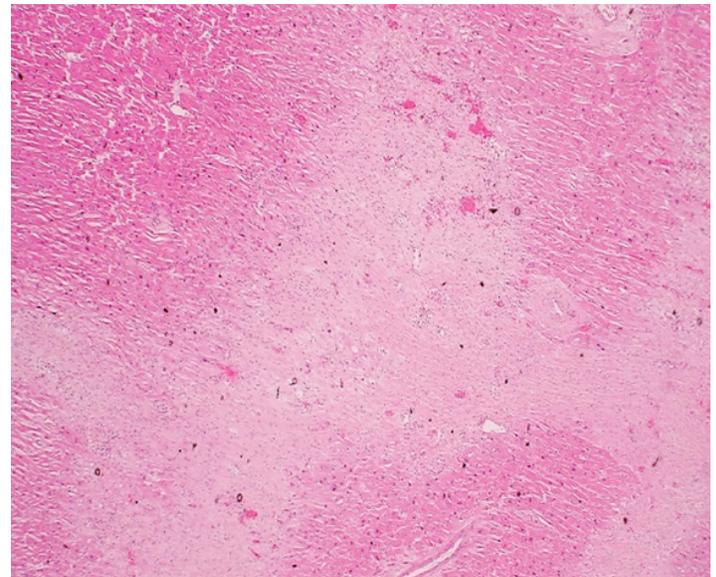
## Results

Patients were three females and 12 males ranging in age from 28 to 78 years ( $\bar{m}=56$ ). Chronic clinical morbidities included depression (8), seizure disorder (4), type II diabetes (2) and hypertension (1). Toxicology results showed lethal-range levels (12) and toxic-range levels (3). Substances included anti-depressants (3), opioids (3), ethanol (2), paracetamol (2), benzodiazepines (1), codeine (1), tramadol (1), fentanyl (1) and weed killer (1). Thirteen cases involved multiple substances (three or more). Gross cardiac findings included severe coronary artery disease (5), dilated cardiomyopathy (3), and left-ventricular hypertrophy (2). Light microscopic cardiac findings were acute and chronic ischemic changes (2), acute myocardial infarction (1) and evidence of heart failure (1). Cause of death was reported as overdose (12) with seven suicides and five accidental cases. Other causes were severe coronary artery disease (1), acute myocardial infarction (1) and drowning (1). Chronic cardiac disease pathology was prevalent in 11/15 (73%) post-mortem overdose cases, while only 3/15

(20%) demonstrated conventional medical risk factors for cardiac disease (not accounting for age). As age can be a risk factor for chronic cardiac disease, decedents age 60 and over were excluded and 8/9 (89%) had chronic cardiac disease pathology, while only three (33%) had conventional cardiac risk factors; diabetes (2) and chronic obstructive pulmonary disease (1) (Figures 1 and 2; mean age = 45 years).



**Figure 1:** Prevalence of cardiac disease risk factors vs. chronic cardiac disease (age 59 years and younger;  $\bar{m}=45$  years).



**Figure 2:** Chronic myocardial ischemic change in 38 yr old male overdose case without other known cardiac risk factors.

## Conclusion

Chronic cardiac disease was prevalent in 73% of post-mortem overdose cases, while only 20% demonstrated conventional medical risk factors for cardiac disease. While substance abuse is a risk factor for cardiac disease, cardiac screening and monitoring is typically not performed without the presence of conventional cardiac risk factors. Cardiac disease screening should be employed

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in substance abuse populations. In this cohort of 15 post-mortem overdose cases, chronic cardiac pathology was observed in 73% of decedents, despite only 20% exhibiting conventional medical risk factors for cardiovascular disease. When younger adults (<60 years) were considered separately, 89% demonstrated structural or histologic cardiac disease, while only 33% had identifiable risk factors such as diabetes or chronic obstructive pulmonary disease. These findings suggest that traditional risk assessment methods may underestimate the prevalence of underlying cardiac disease in individuals with substance use disorders.

Substance exposure was predominantly polypharmacy in nature, with 13 cases involving three or more substances, including opioids, antidepressants, ethanol, benzodiazepines and other agents. The presence of multiple substances, some of which are known to exert cardiotoxic effects (e.g., methadone, fentanyl, tricyclic antidepressants), may increase susceptibility to fatal outcomes in individuals with previously undiagnosed structural heart disease. Post-mortem findings included severe coronary artery disease, dilated cardiomyopathy, left ventricular hypertrophy, and histologic evidence of ischemia and heart failure, highlighting the subclinical nature of cardiac vulnerability in these individuals.

These results align with prior studies demonstrating that opioid and poly-substance use can contribute to silent cardiac pathology. For example, post-mortem investigations have shown high prevalence of cardiac structural changes in opioid and stimulant-related deaths, often in the absence of traditional risk factors [2-4]. Epidemiologic data further indicate that opioid use increases the risk of sudden cardiac arrest independent of previously diagnosed heart disease [6]. Collectively, these findings underscore that substance use itself may act as an independent risk factor for chronic cardiac disease, and that fatal overdose often reflects an interaction between acute toxic exposure and pre-existing cardiac vulnerability.

From a clinical and forensic perspective, these findings highlight the need for broader cardiac screening strategies in substance-using populations. Current guidelines generally focus on conventional risk factors such as hypertension, diabetes, and hyperlipidemia, yet our data suggest that individuals with chronic substance use may harbor silent structural and histopathologic heart disease. Strategies such as ECG monitoring, stress testing, echocardiography, and assessment of cardiac biomarkers could potentially identify at-risk individuals before fatal events occur.

Limitations of this study include the small sample size and retrospective, post-mortem design, which may limit generalizability and preclude definitive causal inference. Additionally, complete clinical histories were not available for all decedents, and toxicological data may not fully capture chronic substance exposure. Despite these limitations, the high prevalence of unrecognized cardiac pathology in this cohort indicates that substance abuse is a clinically important, yet often overlooked, contributor to cardiovascular disease and overdose mortality.

In this cohort of post-mortem overdose cases, chronic cardiac pathology was observed in 73% of decedents, while only 20% had conventional medical risk factors. Among younger adults under 60, 89% showed cardiac disease despite few recognized risk factors. These findings suggest that structural and histopathologic cardiac abnormalities may be common in substance-using populations, even in the absence of traditional risk factors. Poly-substance exposure, including opioids, antidepressants, and ethanol, may interact with underlying cardiac pathology to increase the risk of fatal outcomes. Further research is needed to better clarify the relationship between substance use and subclinical cardiac disease.

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