Methamphetamine-associated cardiovascular conditions in general practice: Screening, management and harm reduction

Cliff Deyo, Sarah Garry, Thileepan Naren, Owen Harris, Casey Grover, Esther Han, David Corbet, Elizabeth Paratz

Background
Methamphetamine use is a prevalent but under-recognised cause of acute and chronic cardiovascular conditions. Deaths from methamphetamine-associated cardiovascular conditions (MACCs) increased seven-fold between 2009 and 2020 in Australia, and MACCs were the leading cause of natural death among people who use methamphetamine. Prognoses for the primary MACCs are optimistic with abstinence and medical management early in disease progression, underscoring the utility of screening; however, screening is underutilised because of unfamiliarity, stigma and lack of guidelines.

Objective
This article provides expert and evidence-based recommendations to guide screening, management and harm reduction relevant to MACCs.

Discussion
Screening for and managing cardiovascular conditions are central concerns for any clinician treating a patient who uses methamphetamine, and a high suspicion of cardiovascular disease is warranted. There should be a low threshold for screening patients with a history of past or present methamphetamine use.

METHAMPHETAMINE is a highly addictive stimulant that has potent cardiotoxic effects.[1,2] Episodic and chronic methamphetamine use has been linked to a range of cardiovascular conditions, notably a dilated-phenotype cardiomyopathy, takotsubo cardiomyopathy, pulmonary hypertension, accelerated coronary artery disease, myocardial infarction, systemic hypertension, hypertensive emergency, arterial vasospasm, aortic dissection, stroke, ventricular arrhythmia and sudden cardiac death.[1,3] Coincident with greater availability of high-purity methamphetamine, deaths from methamphetamine-associated cardiovascular conditions (MACCs) increased approximately seven-fold between 2009 and 2020 in Australia, with MACCs becoming the leading cause of natural death among people who use methamphetamine.[4]

General practice is the primary source of healthcare for people who use methamphetamine.[5] However, a range of barriers prevents people who use substances from receiving medical care, including stigma, trauma and psychosocial disadvantage.[2,3,5–7] Substance use is the most stigmatised health condition globally,[8] and fear of shame in the clinical encounter may deter patients from accessing relevant medical care.[2,8] There are also formidable systemic barriers, including lack of MACCs-specific treatment guidelines and public health policies guiding public awareness and prevention of MACCs.

Objective

Prognoses for methamphetamine-associated cardiomyopathies are optimistic with abstinence and medical management early in disease progression, underscoring the utility of screening.[4,6,9–12] General practice is an ideal setting for screening for and managing MACCs, as general practitioners (GPs) are highly skilled at screening for and managing cardiovascular conditions and interpersonal approaches that foster patient acceptance;[13,14] however, there is a dearth of information to guide general practice. This article provides expert and evidence-based recommendations to guide screening for and management of MACCs, along with key MACCs-related harm-reduction strategies relevant to general practice.

Discussion

Cardiovascular effects of methamphetamine

Methamphetamine's cardiovascular effects are principally attributed to sympathetic overactivation, oxidative stress and direct cell toxicity.[15,16] Acutely, methamphetamine enhances catecholamine activity, increasing heart rate, contractility and blood pressure.[1,4,12,16,17] Severe artery vasospasm and extensive small blood vessel vasoconstriction may contribute to arterial dissection, stroke, myocardial infarction, malignant arrhythmia, acute coronary syndrome, cardiomyopathy and end organ failure.[9,10,16,18] Myocardial infarction may

result from increased oxygen demand from tachycardia and increased contractility in the context of reduced oxygenation due to vasospasm, coronary thrombosis, plaque rupture or co-use of central nervous system and respiratory depressants (eg opiates, sedative medication, alcohol and gamma-hydroxybutyrate).[4,18–20]

The route of administration has not been associated with varying the risk of the primary MACCs (ie cardiomyopathies),[21–23] although systematic evidence and trials in this area are limited. Severity of acute and chronic cardiovascular conditions has been associated with greater dose and frequency of administration, as well as a binge pattern of use.[24,25] In one study, 35% of patients with methamphetamine-associated cardiomyopathy reported less than a month of use.[9]

Screening for MACCs

There should be a low threshold for screening patients with a history of past or present methamphetamine use for MACCs using resting electrocardiography.[26,27] Relevant to screening patients with a past history of methamphetamine use, some MACCs may cause death years after achieving abstinence.[19,21] Electrocardiography screening may also identify patients with non-methamphetamine-associated cardiac conditions associated with sudden cardiac death (eg genetically-acquired hypertrophic cardiomyopathy, short- or long-QT syndromes, Brugada syndrome) for whom methamphetamine use may be catastrophic.

Screening for and early identification of MACCs are critical, as converging evidence from human and animal studies links abstinence with recovery of ventricular function and reverse remodelling in some cases of methamphetamine-associated cardiomyopathy, particularly if fibrosis and chamber remodelling are minimal.[4,6,9–12] Screening is also supported by Australian research reporting significant cardiovascular disease in half of coronial cases of methamphetamine-related deaths.[21] Another study reported abnormalities on 72% of electrocardiographs of hospital patients who use methamphetamine (n = 106): left ventricular hypertrophy (26%), lateral T-wave inversion (4%), p-pulmonale pattern (8%), inferior Q waves (10%), right axis deviation (8%) and prolonged QT interval corrected (QTc) for heart rate (27%).[27] A subsample (n = 24) had transthoracic echocardiography: abnormalities included severe left ventricular dysfunction (38%), left ventricular thrombus/spontaneous echocontrast (9%), right ventricular dysfunction (33%) with left ventricular dysfunction or pulmonary hypertension, left atrial dilation (42%), right atrial dilation (13%) and severe pulmonary hypertension (13%). Moderate-to-severe valvular regurgitation and endocarditis were also prevalent. The electrocardiographs were primarily for elective procedures,[27] so the findings may generalise reasonably well to patients who present to general practice.

Prolongation of QTc is a common electrocardiogram finding among patients who use methamphetamine (24–34%) and may reflect polypharmacy or prognosticate for torsades de pointes and sudden cardiac death.[1,26,27,28–30] Some common formulas overestimate QTc at higher heart rates,[31] which is a concern if the heart rate is elevated because of acute methamphetamine effects. When there is concern regarding interpretation of QTc, cardiology review of electrocardiograms prior to decision making regarding QTc-prolonging medications is recommended, and multidisciplinary discussion of the importance of the concomitant medication may be required.

Investigating suspected MACCs

Guidelines recommend an elevated degree of suspicion for cardiovascular conditions among patients with long-term or heavy stimulant use, a lower threshold for cardiac evaluation based on patient history and physical exam, and a low threshold for transthoracic echocardiography for symptomatic patients.[32] Work-up for any suspected MACC follows the corresponding standard clinical guideline. MACCs should be considered in the differential diagnosis of young patients with cardiac or pulmonary symptoms irrespective of whether they report methamphetamine use.

GPs can order Medicare Benefits Schedule–funded N-terminal prohormone of brain natriuretic peptide (NT-proBNP) testing to investigate suspected heart failure and assist with decision making regarding transthoracic echocardiography:[33] the result should be used to guide decision making according to guidelines. A negative NT-proBNP result should not preclude transthoracic echocardiography: NT-proBNP is very good at identifying cardiac stress and congestive cardiac failure, but it is important to note that this marker can be in the normal range in patients with compensated left ventricular systolic dysfunction.[34]

Medical management of MACCs

Although abstinence is vital to reverse, arrest or slow progression of MACCs, medical management also plays an important part.[4,6,9–12] Medical management for any MACC follows the corresponding standard clinical guideline.[3,6] In the case of methamphetamine-associated cardiomyopathy, medical management is guideline-directed medical therapy for heart failure,[3,6,11,28,35] and patients should have cardiology input.

Key considerations regarding the management of MACCs include enhancing adherence and reducing risk of adverse effects of common medications used to manage some MACCs. Many people who use methamphetamine have difficulty with polypharmacy, attending appointments and reducing their methamphetamine use because of competing needs (eg homelessness, social isolation and mental health) and other concerns (eg medication cost, appointment burden): encourage patients to self-refer as appropriate to specialist alcohol and other drug, mental health and community health services.

SGLT-2 inhibitors, heart failure and methamphetamine use

Sodium-glucose co-transporter-2 (SGLT-2) inhibitor-mediated euglycaemic ketoacidosis is an uncommon but life-threatening adverse effect due to reduced nutritional intake or reduced carbohydrate absorption while taking SGLT-2 inhibitors. It is characterised by high ketone levels and metabolic acidosis despite normal to mildly elevated plasma glucose.[36–38] This concern is pertinent when prescribing to patients who use methamphetamine because of their reduced oral intake and increased exertion and physical stress, which are common during methamphetamine use.[6] Additional risk factors to consider include

low body mass index, sarcopenia, older age, alcohol consumption, pregnancy,[38] infection, surgery and dehydration. Patient education should be provided about mechanisms and symptoms of euglycaemic ketoacidosis as well as advice regarding regular food intake and rest when using methamphetamine.[38]

Treatment of methamphetamine use disorder

There is no approved pharmacotherapy to aid reduction or abstinence, or to prevent relapse in methamphetamine use disorder,[2,4,39,40] and the safety of pharmacotherapies has not been shown in phase III clinical trials.[39] Contingency management (ie vouchers and other rewards are given for achieving target behaviours such as attending appointments) combined with cognitive behavioural therapy or other psychosocial intervention has the best evidence base.[2,3,39]

Harm reduction

Prevention and treatment of MACCs are centred on cessation or reduction of methamphetamine use; however, many patients will not be ready to change their pattern of use or will need to address other concerns as a priority, such as homelessness, financial issues and mental health. Discussion of harm-reduction strategies (Box 1) is an important intervention for these patients.[2,4,5,8,20,35,39–41]

Methamphetamine overdose death is a growing concern in Australia, as some evidence indicates a nearly five-fold increase in non-intentional methamphetamine overdose deaths between 2010 and 2020.[4] The increase in overdose deaths may relate to ease of availability of high-potency methamphetamine,[4] acute effects of methamphetamine in the context of MACCs[4,41] and co-use of methamphetamine with central nervous system and respiratory depressants.[4,18–20] Some evidence more strongly associates the increase in overdose deaths with older age, possibly reflecting the cumulative cardiovascular effects of ageing and chronic methamphetamine use.[4] GPs might help to prevent overdose death by screening for and managing MACCs (ie reducing cardiovascular vulnerability as an overdose risk factor), educating patients about the risk of co-use with central nervous system and respiratory depressants, and encouraging patients to self-refer to specialist alcohol and other drug services. We are unaware of evidence indicating increased overdose risk after a period of abstinence. The 'toxic dose' that produces serious cardiovascular effects or death is unknown and might relate to individual differences in response, tolerance or underlying cardiovascular disease (eg MACCs), so assessment of acute risk may be best assessed on the basis of presentation.[22,24] Any amount of methamphetamine use carries risk: even small doses have been associated with death.[22]

Conclusion

As MACCs are the leading cause of natural death among people who use methamphetamine,[4] preventing and managing cardiovascular conditions are key clinical priorities.[3] Given the low public awareness of MACCs, a non-judgemental conversation with a GP may be the first time patients learn about the significant cardiovascular impacts of methamphetamine use. Such discussions can open the door to appropriate screening and empower patients to make positive changes.

Box 1. Cardiovascular-related harm-reduction strategies

- Inform patients about methamphetamine-associated cardiovascular conditions.
- Provide education about symptoms/signs of stroke and acute coronary syndrome.
- Discuss which drug–drug interactions (prescribed and non-prescribed) increase overdose risk and suggest avoiding these combinations.
- Advise regular breaks in use: repeated dosing over days amplifies cardiovascular effects.[42]
- Inform patients that using smaller amounts, less often may cause less cardiovascular harm.[22]
- Recommend use with other people present so they can respond to overdose.
- Address modifiable cardiovascular risk factors: smoking, hypertension, hypercholesterolaemia, chronic kidney disease, etc.[43]

Key points

- Elevated suspicion of cardiovascular disease is warranted among patients who use methamphetamine.
- Screening, abstinence and medical management of the underlying cardiovascular condition are key to cardiac recovery.
- A low threshold is warranted for electrocardiography screening in patients with past or present methamphetamine use, and for transthoracic echocardiography in symptomatic patients.
- Medical management for any MACC follows the corresponding standard clinical guideline.

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