Clozapine Initiation in a Patient with Cardiomyopathy

Luke Klugherz, M.D., Pharm.D.[1], Jonathan G. Leung, Pharm.D.[2], Laura Suarez, M.D.[1]
[1]Division of Psychiatry and Psychology, Mayo Clinic, Rochester, MN, [2]Department of Pharmacy, Mayo Clinic, Rochester, MN.

ABSTRACT

BACKGROUND/SIGNIFICANCE
There is limited literature guidance – one case report (Sanchez et al., 2016) – on the usage of clozapine for psychotic illness in patients with cardiomyopathy.[1] We present a case that offers an interdisciplinary approach involving psychiatry, cardiology, and pharmacy in the decision-making process and monitoring of clozapine initiation in a patient with previously diagnosed cardiomyopathy.

CASE
A 35-year-old gentleman with history of treatment-resistant schizophrenia and idiopathic cardiomyopathy (left ventricular ejection fraction (LVEF) 29% three years prior to admission) was admitted to the inpatient psychiatric hospital after 1 week of worsening psychosis and functional decline. He was reportedly adherent to long-acting injectable paliperidone and perphenazine. Previous electroconvulsive therapy caused sinus bradycardia and pause, and his known cardiomyopathy had precluded a clozapine trial. His case was discussed with cardiology colleagues who recommended baseline electrocardiogram (ECG) (sinus arrhythmia; QTc 450 ms), baseline troponin (normal), and repeating echocardiography; this showed interval normalization of LVEF (54%) with normal systolic and diastolic function. Clozapine monotherapy was initiated. Cardiology and pharmacy assisted with a plan to monitor for cardiotoxicity including daily assessment of vitals, weight, and cardiac symptoms, weekly ECG, and weekly C-reactive protein (CRP) to screen for myocarditis. ECG on clozapine day 4 showed normal sinus rhythm with QTc 436 ms, and CRP was unremarkable on clozapine days 12 and 19. He developed mild orthostatic hypotension and tachycardia which resolved after dose reductions of previous lisinopril, metoprolol succinate, and furosemide. Steady-state clozapine level was 353 ng/mL. His psychosis and independent function improved significantly, and he was discharged home. Repeat echocardiography at 6 and 12 months was recommended. He was psychiatrically stable and showed no cardiotoxicity 4 months after hospitalization.

DISCUSSION
In this case, clozapine was used to manage treatment-resistant psychotic illness in a patient with cardiomyopathy. Previously deferred clozapine trials likely led to polypharmacy and suboptimal psychosis management. Siskind et al., 2020 found that clozapine-induced myocarditis (0.7%) and cardiomyopathy (0.6%) are rare, though myocarditis is more likely to be fatal (12.7%).[2] The risks of suboptimally treated psychosis needed to be balanced against clozapine-associated cardiovascular sequelae. The interdisciplinary collaboration was necessary to discuss risks and benefits; his interval echocardiographic improvement implied improved cardiac reserve and reduced mortality risk. Having this knowledge enabled us to jointly initiate clozapine. Recent guidelines suggest baseline cardiovascular studies, daily monitoring of cardiovascular symptoms, and weekly CRP and troponin tests for two months (Correll et al., 2022).[3] There was no interval evidence of myocarditis or cardiomyopathy in our case.

CONCLUSION/IMPLICATION
In patients with previously diagnosed cardiomyopathy, liaison between psychiatry, cardiology, and pharmacy can facilitate appropriate cardiovascular risk stratification and safe clozapine initiation.

PATIENT FACTORS

35-year-old single, unemployed man admitted with worsening psychosis

Diagnoses: schizophrenia (treatment resistant), binge eating disorder (treated), nicotine dependence

Medical problems: idiopathic heart failure with LVEF 29% two years before admission, prolonged QT interval, urinary retention, tremor, ECG: sinus arrhythmia and QTc 433 ms

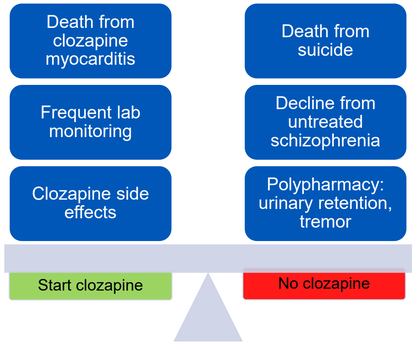
Meds on admission: Paliperidone LAI 234 mg IM every 28 days (last dose week before admit), perphenazine 16 mg/day, lithium 900 mg/day, escitalopram 10 mg, trihexyphenidyl 4 mg/day

Previous treatments

- risperidone, olanzapine, quetiapine, lurasidone, aripiprazole, perphenazine, PRN haloperidol
- clozapine not tried with concern for weight gain and cardiomyopathy
- 4 bitemporal ECT treatments stopped due to “sinus bradycardia and pause” (cardiology involved)

RISK-RISK ASSESSMENT

FIGURE 1



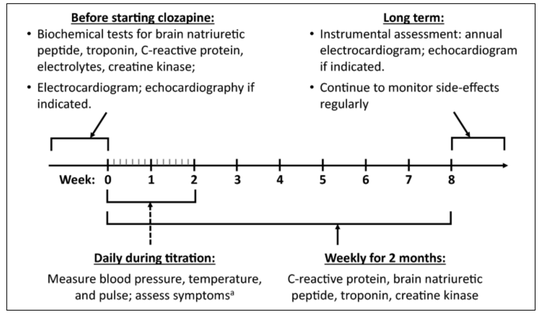
Risk assessment of starting clozapine compared to not starting clozapine.

CLOZAPINE AND THE HEART

TABLE 1: Clozapine-induced myocarditis vs cardiomyopathy[2]

	Myocarditis	Cardiomyopathy
Timeline	Usually first month (time dependent)	Months – years (time dependent)
Rate	0.7% (95% CI 0.3–1.6%)	0.6% (95% CI 0.2–2.3%)
Symptoms	Variable, often non-specific: fever/chills, malaise, tachycardia/palpitations, arrhythmias, chest pain, fluid overload, or asymptomatic	↓ exercise tolerance, edema, shortness of breath, arrhythmias
Clinical findings	• fever (67%) • troponin >2x ULN (90%) • CRP > 100 mg/dL (70%) • eosinophilia (50% cases vs 30% controls) • definitive dx myocardial biopsy or cMRI (75% sensitivity) • ECG not sensitive	• ↑ BNP / pro-BNP • fluid overload on exam • abnormal echocardiography
Mortality	12.7-64%	7-8%

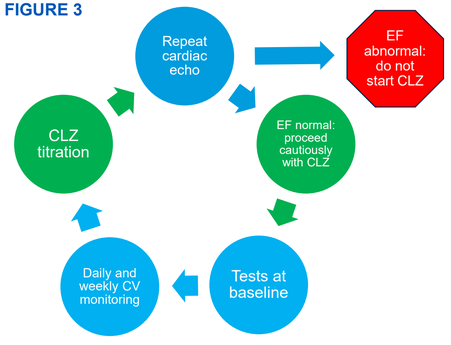
FIGURE 2



Correll et al. recommended cardiovascular monitoring parameters during clozapine initiation.[3]

HOSPITAL COURSE

FIGURE 3



Recommended approach by cardiology for cardiovascular decision-making with clozapine.

Baseline: Interval normalization of LVEF (54%) with normal systolic and diastolic function, normal troponin. Paliperidone, perphenazine, lithium discontinued.

HD5: Clozapine 50 mg/day. Endorsed many physical symptoms including chest pain, tachycardia. Normal vitals. ECG unremarkable.

HD10: Clozapine 125 mg/day. Mood improving. Mild hypotension 99/61 mm Hg.

HD15: Clozapine 150 mg/day. Better thought organization. Orthostatic symptoms so furosemide discontinued. Urinary retention resolved with discontinuation of trihexyphenidyl.

HD20: Clozapine 200 mg/day. Only mild auditory hallucinations. CRP normal.

HD22 (discharged home): Clozapine 200 mg/day, trough level 353 mg/dL. Hallucinations “drastically better.” No clinical concern for myocarditis or cardiomyopathy. No more issues with orthostatic symptoms with dose reductions of antihypertensive medications.

POST-HOSPITAL COURSE

1 month: Feeling well, reading, practicing languages.

3 months: “continues to do much better with clozapine compared to prior antipsychotics.” Exercising and losing weight per his goal while taking metformin.

10 months: No physical or mental health concerns. Antihypertensive reduced to lowest possible dose. Planning for repeat echocardiography at 12 months.

CONCLUSIONS / DISCUSSION

- Risks of untreated severe mental illness must be thoughtfully weighed against risks of medications and comorbidities
- Myocarditis (earlier onset) and cardiomyopathy (later onset) caused by clozapine are both rare; myocarditis is more likely to be fatal
- When clozapine is started in patients with cardiovascular disease, understanding base rates and collaboration with cardiology can be very helpful for decision-making and optimal care
- There are recommended guidelines to monitor for clozapine-induced myocarditis, and pharmacists can assist with creating and implementing this plan
- History of cardiovascular disease should not be an absolute contraindication to starting clozapine; patients may be able to benefit safely from clozapine with appropriate use and monitoring

REFERENCES / DISCLOSURES

1. A. Y. Sanchez, et al. Clozapine in a patient with treatment-resistant schizophrenia and hypertrophic cardiomyopathy: a case report. BJPsych Open. Nov 2016.
2. D. Siskind, et al. Systematic review and meta-analysis of rates of clozapine-associated myocarditis and cardiomyopathy. Aust N Z J Psychiatry. May 2020.
3. C. U. Correll, et al. A Guideline and Checklist for Initiating and Managing Clozapine Treatment in Patients with Treatment-Resistant Schizophrenia. CNS Drugs. Jul 2022.

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