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Short Commentary

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Seeing complexity clearly: Integrating clinical imaging with polypharmacology in chronic disease management

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Abstract

Chronic diseases often emerge from multifactorial pathogenesis and interconnected biological pathways, making single-target treatments insufficient for long-term control. Polypharmacology-modulating multiple targets with a single agent or combination therapy-offers a promising alternative. Yet its clinical application remains largely pharmacokinetic. In this Perspective, we argue that integrating clinical imaging with polypharmacology can elevate chronic disease management, providing real-time feedback on drug efficacy, organ-level response, and systemic burden. Through five case vignettes-hypertension, diabetes, obesity, atherosclerosis, and COPD-we illustrate how visual biomarkers, from echocardiograms to CT angiograms, can guide the deployment and personalization of multitarget therapeutics.

Keywords: Polypharmacology; Multitarget drugs; Clinical imaging; Chronic disease; Multimorbidity; Visual biomarkers; Personalized therapy.

Introduction

Polypharmacology meets visual medicine

Chronic diseases are characterized by long-term duration and complex pathophysiological processes. They often involve multiple interconnected molecular pathways and cellular functions. The traditional "magic bullet" paradigm-one drug, one target-has faltered in the face of chronic diseases characterized [1]. Polypharmacology, the intentional modulation of multiple biological targets by a single drug or drug combination, addresses this gap by disrupting multiple nodes within disease networks [2-7]. Drugs like SGLT2 inhibitors, GLP-1/GIP agonists, and Arnie exemplify this trend, offering pleiotropic benefits in diabetes, heart failure, and obesity. However, the implementation of polypharmacology remains largely biochemical. What if visual cues could enhance therapeutic precision? Clinical images-from chest radiographs to echocardiograms and MRI scans-offer anatomical and functional insights that mirror pathophysiology [8-12]. Their integration with Polypharmacology strategy enables clinicians to match mechanism with morphology, optimizing treatment in real time. The following cases illustrate this synergy.

Case vignettes: Imaging meets polypharmacology.

1. Hypertension-A silent web of risk: Mr. A, a 68-year-old man with stage 2 hypertension and early-stage chronic kidney disease, is started on an Angiotensin Receptor Blocker (ARB). Despite blood pressure reduction and normal ejection fraction, albuminuria and left ventricular hypertrophy persist

The echo reveals concentric hypertrophy and diastolic dysfunction-morphological markers that don't reverse with BP lowering alone. While ARBs effectively lower systemic blood pressure, they lack direct antifibrotic or anti-inflammatory actions. In contrast, sacubitril/valsartan (ARNi) not only reduces pressure afterload but also counter maladaptive neurohormonal signaling, offering broader cardiovascular and renal protection. Follow-up echo shows regression in wall thickness and improved compliance. Imaging validates multitarget therapy.

2. Type 2 Diabetes-More than glucose control: Mrs. B, a 59-year-old with type 2 diabetes and mild proteinuria, presents with lower limb edema and fatigue. Cardiac MRI reveals subclinical myocardial fibrosis.

Glucose-centric therapies may normalize HbA1c but fail to address the cardiorenal-metabolic axis with tissue-level damage progressing. Initiation of empagliflozin not only stabilized renal function but halted fibrotic remodeling, seen as reduced late gadolinium enhancement on follow-up MRI. Here, imaging directs escalation to multitarget therapy beyond glycemia. Moreover, empagliflozin lowered glucose, induced weight loss, reduced intraglomerular pressure, and provided heart failure protection-demonstrating the power of a multitarget approach.

3. Obesity-Imaging the metabolic burden: Ms. C, a 44-year-old with morbid obesity and metabolic syndrome, undergoes abdominal MRI, revealing hepatic steatosis and increased visceral fat. Monotherapy targeting appetite suppression or lipid metabolism alone yields marginal weight loss. Introduction of tripeptide (GLP-1/GIP agonist) results in marked weight reduction, decreased liver fat content, and normalized ALT levels. These agents redefine obesity as a multisystem disorder treatable through coordinated metabolic modulation. Imaging quantifies therapeutic efficacy and systemic benefit, aligning with multitarget action on glucose, appetite, and lipid metabolism.

4. Atherosclerosis-A battle on many fronts: Mr. D, a 72-year-old with peripheral artery disease, is on statins but has persistently elevated hsCRP and stable but thick Carotid Intima-Media Thickness (CIMT) on ultrasound. Intensifying LDL-lowering with bempedoic acid + ezetimibe leads to plaque regression seen on serial carotid ultrasound. Residual inflammation prompts the addition of low-dose colchicine or PCSK9 inhibitors. This illustrates dual-imaging and dual-therapy strategy: anti-lipid and anti-inflammatory, with CIMT as a dynamic biomarker.

5. COPD-Beyond bronchodilation: Mr. E, a 65-year-old ex-smoker with COPD and metabolic syndrome, showed emphysematous changes and air trapping on HRCT. Single bronchodilators may reduce symptoms but do not address systemic inflammation or comorbid risks. Triple therapy combinations (LAMA + LABA + ICS) offer multitargeted control of airway tone, inflammation, and mucosal remodeling. Moreover, Introduction of roflumilast, a PDE4 inhibitor with anti-inflammatory properties, leads to reduced exacerbation frequency and improved lung volumes on follow-up imaging. Functional CT and spirometry guide multitarget pharmacologic layering, beyond bronchodilation.

Discussion

Toward imaging-guided polypharmacology: Chronic diseases no longer behave as siloed organ conditions; they are interlinked biological syndromes. The traditional model of escalating monotherapies leads to polypharmacy, reduced adherence, and increased adverse events. In contrast, rationally designed multitarget drugs or fixed-dose combinations may optimize outcomes, reduce pill burden, and improve compliance [1-7]. Imaging provides a window into target engagement that lab tests alone cannot offer. Whether through reverse remodeling on echocardiogram, fibrosis reduction on MRI, or plaque regression on ultrasound, visual biomarkers validate the systemic impact of multitarget drugs [8-12]. Moreover, imaging helps detect off-target organ stress early (e.g., cardiac MRI in diabetic cardiomyopathy), select patients most likely to benefit from polypharmacology (e.g., high-risk CIMT profiles), and adjust or de-escalate therapy based on morphological response. As chronic diseases increasingly present as network disorders, the integration of network-based therapeutics with network-informed imaging becomes a powerful clinical framework.

Conclusion

The convergence of polypharmacology and clinical imaging represents a new frontier in chronic disease management. By pairing mechanism-driven multitarget drugs with morphology-driven visual feedback, clinicians can deliver more precise, effective, and personalized care. In a field often dominated by numbers, images remind us that seeing is still believing.

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