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Looking inside the heart: how multiple chronic illnesses disrupt our cells

The aim of this study was to understand how having several ongoing health problems—what we refer to as multimorbidity—impacts the heart in people with cardiovascular disease, especially those undergoing heart surgery. Multimorbidity is becoming more common, particularly in older adults, and it's well known that patients with multiple conditions often face worse outcomes in hospital settings. However, the biological reasons behind this are still not fully understood. Therefore, we explored what is happening inside the body at a deeper level—not just looking at usual health risk factors like blood pressure or cholesterol, but at what's going on inside the heart's cells.

To do this, 144 patients scheduled for heart surgery were enrolled into our study. Among them, 98 had two or more long-term conditions, such as diabetes, kidney disease, or chronic lung disease. We have collected and analysed samples from their heart tissue, blood, and immune cells. Using advanced techniques such as gene expression profiling, metabolomics, and mitochondrial respiration assays, we have attempted to build a detailed picture of what was happening inside the cells of these individuals.

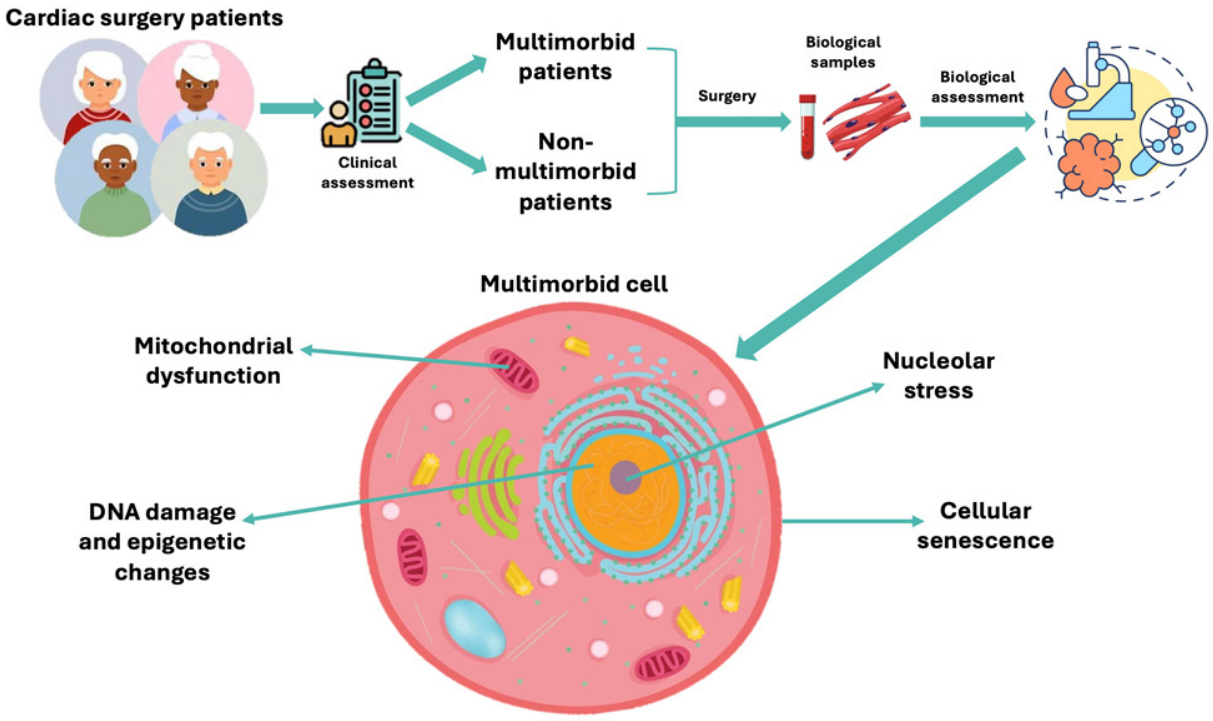

Fig. 1 .Overview of the clinical and biological investigation of multimorbidity in cardiac surgery patients. Patients undergoing heart surgery were clinically assessed and categorized into multimorbid (≥2 chronic conditions) and non-multimorbid groups. Biological samples, including blood and heart tissue, were collected during surgery for in-depth molecular analysis. Key cellular alterations identified in multimorbid patients included mitochondrial dysfunction, nucleolar stress, DNA damage with associated epigenetic changes, and increased cellular senescence.

One of the key findings was that multimorbidity is associated with DNA damage in heart cells. Specifically, the researchers observed increased expression of genes related to histones (proteins that help package DNA) and enzymes involved in DNA repair, indicating that the cells were under stress and trying to maintain genetic stability. They also found evidence of nucleolar stress, which affects the part of the cell responsible for producing ribosomes—structures essential for making proteins. This kind of stress is known to disrupt normal cell function and is often seen in aging or diseased cells.

In addition to DNA damage, the study identified problems with mitochondrial function in patients with multimorbidity. Mitochondria are the energy powerhouses of cells, and in these patients, mitochondria were less efficient at producing energy. This was evident in both heart tissue and circulating immune cells. Impaired mitochondrial activity means that cells are less able to meet energy demands, especially during the physical stress of surgery, which could explain the increased vulnerability of these patients.

Another key finding was the presence of cellular senescence – a state in which cells stop dividing and begin to secrete harmful molecules that promote inflammation and tissue damage. Molecules such as IL-1β and GM-CSF—both linked to aging and chronic inflammation—were elevated in the blood of multimorbid patients. These senescent and inflamed cells may further impair healing and organ function after surgery.

Overall, the study provides compelling evidence that multimorbidity is not just a clinical label—it corresponds to real, measurable damage at the cellular level in the heart. These patients' cells are showing signs of accelerated aging, energy failure, immune dysfunction, and genetic instability. The biological changes identified in this research may help explain why patients with multimorbidity often have worse outcomes during and after heart surgery.

Understanding these mechanisms opens the door to new types of treatments. For example, therapies aimed at protecting DNA, reducing nucleolar and cellular stress, or boosting mitochondrial energy production might improve surgical recovery and long-term heart health in people with multiple chronic illnesses. By revealing the hidden toll that multimorbidity takes on the heart, this study highlights the importance of addressing not just the primary disease, but the broader biological challenges that come with living with several long-term conditions.

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