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Clonal haematopoiesis of indeterminate potential as a driver of adverse left ventricular remodeling after ST-elevation myocardial infarction

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Abstract

Objective: This study aims to explore the relationship between clonal haematopoiesis of indeterminate potential and poor adverse left ventricle remodeling in ST-elevation myocardial infarction. **Methods:** This was a prospective cohort of 340 patients with ST-Elevation Myocardial Infarction (STEMI) who presented for primary Percutaneous Coronary Intervention (PCI) and were screened for clonal haematopoiesis (VAF $\geq 2\%$) with targeted Next-Generation Sequencing (NGS) having a Cardiac Magnetic Resonance imaging (CMR) examination at baseline and at 6 months. An increase in E.D.V.I. $\geq 20\%$ was thought to represent adverse remodeling. Cox regression was used in a multivariable logistic regression framework to test the definition of inflammatory markers of the association with clonal haematopoiesis and major cardiovascular events. **Results:** Clonal haematopoiesis was detected (typically for DNMT3A) in 69 patients. Carriers were found to have greater concentration of interleukin-6, microvascular obstruction and infarcts than non-carriers (all $p < 0.001$). 70% of carriers and 25% of non-carriers had adverse remodeling, which was independently associated with clonal haematopoiesis after adjustment for infarct size, microvascular obstruction, anterior infarction as well as age and diabetes. Association was observed over the most common genes. During follow-up, there was a greater frequency of Major Adverse Cardiovascular Events (MACE) in carriers ($p < 0.001$). **Conclusion:** Independently of regular monitoring of CHIP was associated with adverse LV remodeling and prognosis after STEMI, as expected. Screening could prove patients with clonal haematopoiesis are sensitive to targeted anti-inflammatory therapy and that they may be at risk of developing heart failure in the wake of an infarction.

Keywords: Clonal haematopoiesis, CHIP, ST-elevation myocardial infarction, Heart failure, Inflammation, Cardiac magnetic resonance

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1. Introduction

Progressive enlargement of the Left Ventricle (LV) and dysfunction, termed elevated left ventricular remodeling (LVE), is seen in many survivors of ST-Elevation Myocardial Infarction (STEMI) and predates, and predicts,

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Heart Failure (HF) (Bolognese *et al.*, 2002; Bulluck *et al.*, 2018). Remodeling depends upon the extent of the infarct and any injury that happens during re-perfusion, so the amount of inflammation that occurs following the contamination of the re-perfusion will affect remodeling (de Waha *et al.*, 2017).

Despite today's reperfusion therapy, heart failure is a frequent and important complication of myocardial infarction and the heart failure population after an infarct has a poor prognosis, high mortality, and is a major component of the burden of heart failure. If a marker was measurable on a routine blood sample that could identify those patients at the time of the infarct who were most likely to remodel and progress to heart failure, they might be measured more closely and intervene sooner than is currently being done. The genomic aberration known as 'clonal haematopoiesis of indeterminate potential' is such a candidate, because it is a simple to detect aberration with levels that correlate with inflammatory pathways controlling the remodeling of the ventricle. Clonal haematopoiesis of indeterminate potential has emerged as a determinant of that inflammatory response. Ageing, haematopoietic stem cells accumulate somatic mutations, with the most frequent mutations in epigenetic factors DNMT3A and TET2 and the emergence of a mutant clone to a measurable proportion of the circulating blood cells in an individual without haematological malignancy or cytopenia (Genovese *et al.*, 2014; Jaiswal *et al.*, 2014; Steensma *et al.*, 2015). This is a common trait, where the frequency of the variant allele is at least two percent, which usually appears later in life and has been associated with increased risk for atherosclerotic cardiovascular disease (ASCVD) and Heart Failure (HF), independent of conventional risk factors (Jaiswal *et al.*, 2017; Libby *et al.*, 2019).

The mutation and the myocardium is linked via the inflammatory mechanism. In experimental models, macrophages lacking Tet2 or Dnmt3a are hyper-responsible, with excessive activation of the NLRP3 inflammasome and release of excessive levels of interleukin-1 beta and interleukin-6, which leads to rapid rates of atherosclerosis and increased cardiac remodeling and fibrosis following injury (Fuster *et al.*, 2017; Sano *et al.*, 2018; Abplanalp *et al.*, 2021). In a patient already having heart failure, the mutated persons have a poorer prognosis, the larger the clone (Dorsheimer *et al.*, 2019; Assmus *et al.*, 2021). Clonal haematopoiesis is a potential mechanism for remodelling post myocardial infarction, as the same inflammatory pathways are also involved in healing of the infarct, but has not been extensively described in the acute setting (Heimlich and Bick, 2022).

In this study, researchers set out to determine if the development of clonal haematopoiesis led to adverse left ventricular remodeling following ST-Elevation Myocardial infarction (STEMI). It established the prevalence and spectrum of clonal haematopoiesis in a prospective cohort of patients undergoing primary percutaneous coronary intervention and serial cardiac magnetic resonance imaging, gave comparisons of infarct characteristics, inflammatory state and remodeling between carriers and non-carriers, tested for the independence of the association of clonal haematopoiesis with adverse remodeling and looked for a relationship with major adverse cardiovascular events.

2. Materials and methods

2.1. Study design and setting

A prospective cohort study was performed at a tertiary care hospital, where a primary Percutaneous Coronary Intervention (PCI) service is also available, in the department of cardiovascular medicine. All patients who presented with STEMI were consecutively recruited, and after reviewing their clinical data, periodic cardiac imaging was performed. The study design and reporting were based on the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (von Elm *et al.*, 2007).

2.2. Patients and eligibility

Adults with a first ST-elevation myocardial infarction treated by primary percutaneous coronary intervention, in accordance with the prevailing guidelines, were eligible (Byrne *et al.*, 2023). Patients with known haematological malignancy or cytopenia, a history of myocardial infarction, or contraindication to cardiac magnetic resonance imaging, or who had an inflammatory disease or other malignancy that would interfere with the assessment of inflammation were excluded. Total of 340 patients were entered.

2.3. detection of clonal haematopoiesis

A blood sample was obtained at a peripheral blood site for collection at the time of the index admission, and DNA was extracted from the blood cells and then submitted for targeted Next-Generation Sequencing (NGS) of a panel of genes that are recurrently mutated in CH, such as DNMT3A, TET2, ASXL1, JAK2 and TP53. All clones were considered clonal haematopoiesis of indeterminate potential (C-HIP) in the absence of haematological malignancy or haematological cytopenia if the proportion of the VAF was $\geq 2\%$ or large clonal haematopoiesis clone if VAF was $\geq 10\%$.

2.4. Cardiac Magnetic Resonance (CMR) and definition of remodeling

At admission and at 6 months after the CHOI trial, cardiac MRI was requested. LV end-diastolic (LVEDV) and end-systolic (LVESV) volume indices and intraventricular EF were measured and infarct size and whether microvascular obstruction occurred were determined by late Gd enhancement. The primary endpoint was adverse left ventricular remodeling according to the universally accepted imaging endpoint of pathological dilation as $>20\%$ increase in left ventricular end-diastolic volume index (LVEDVi) from the baseline measurement to the 6-month scan.

2.5. Inflammatory biomarkers

Interleukin-6 and high-sensitivity C-reactive protein were measured from the admission sample as indices of the systemic inflammatory response, the pathway through which clonal haematopoiesis is thought to act.

2.6. Statistical analysis

The t-test or the chi-squared test was used to compare carriers and non-carriers according to clonal haematopoiesis as appropriate. Multivariable logistic regression on the association of clonal haematopoiesis with adverse remodeling, including the infarct size, microvascular obstruction, anterior infarction, age and diabetes, was performed and the odds ratio from the multivariable model with its 95% Confidence Interval (CI) was reported. The association with major adverse cardiovascular events was assessed by the Kaplan-Meier method, the log-rank test and Cox proportional-hazards regression. Two sided probabilities of less than 0.05 was considered significant.

3. Results

3.1. Cohort and clonal haematopoiesis

Overall, the study included 340 STEMI patients treated with first-line PCI. In 69 patients (20%) there was clonal haematopoiesis of indeterminate potential, with a median VAF of 8.7%, with the most common gene involved being DNMT3A, followed by TET2 and ASXL1 (Figure 1). As would be expected the carriers were older than the non-carriers, and a higher proportion of the former cohort had diabetes (Table 1).

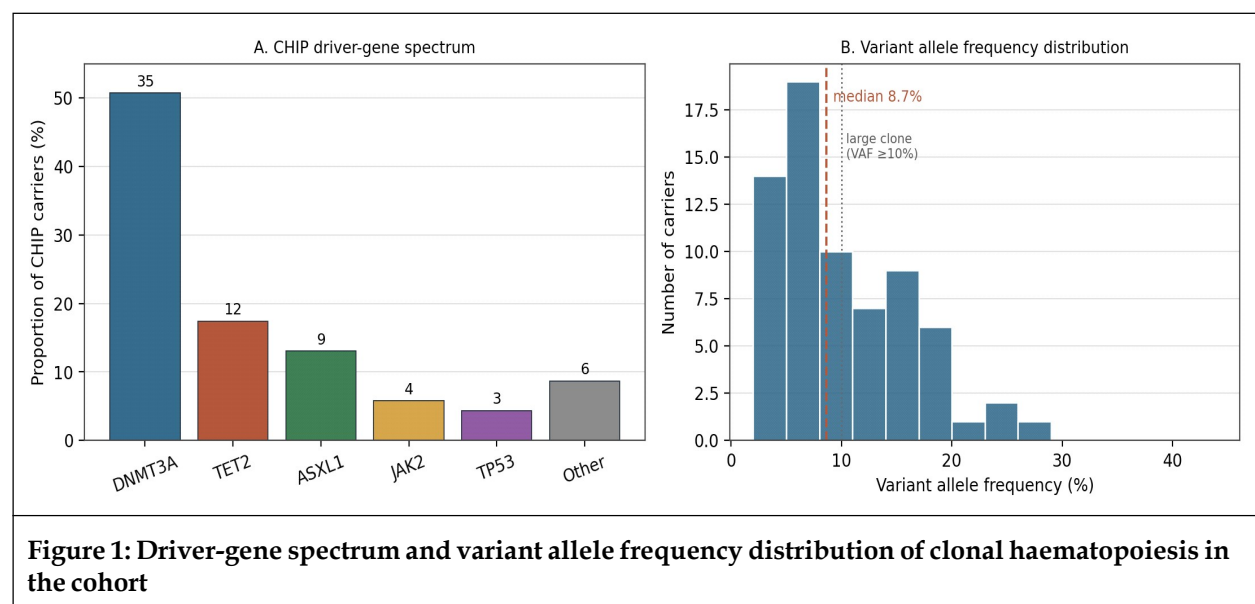


Table 1: Baseline characteristics of carriers and non-carriers of clonal haematopoiesis

Characteristic	CHIP (n = 69)	No CHIP (n = 271)	p
Age (years)	65.8 ± 7.8	59.4 ± 9.3	<0.001
Male sex	51 (74%)	200 (74%)	1.000
Diabetes mellitus	27 (39%)	75 (28%)	0.088
Hypertension	36 (52%)	164 (61%)	0.263
Anterior STEMI	30 (43%)	120 (44%)	1.000
Pre-PCI TIMI 0/1	38 (55%)	170 (63%)	0.304
Symptom-to-balloon (min)	232.1 ± 88.0	210.8 ± 75.0	0.043
GRACE score	145.6 ± 28.8	137.6 ± 28.1	0.038

3.2. Infarct characteristics and remodeling

Carriers of clonal haematopoiesis sustained more severe infarcts. Their infarct size was larger, microvascular obstruction was more frequent, and their interleukin-6 and C-reactive protein levels were higher than those of non-carriers, consistent with the greater inflammatory response that the condition confers; the interleukin-6 level was 8.3 pg/mL in carriers against 5.5 pg/mL in non-carriers. At 6 months the left ventricular end-diastolic volume index had increased more in the carriers, and adverse remodeling occurred in 57% of carriers against 24% of non-carriers. These measures are given in Table 2. The larger infarct, the greater microvascular obstruction and the higher inflammatory markers together describe the pathway through which clonal haematopoiesis acts on the ventricle, and the greater dilation is its structural consequence.

Table 2: Infarct characteristics, inflammatory markers and left ventricular remodeling by clonal haematopoiesis status

Measure	CHIP	No CHIP	p
Infarct size (% LV)	21.9 ± 7.2	19.0 ± 6.7	0.002
Microvascular obstruction	29 (42%)	85 (31%)	0.125
Baseline LVEDVi (mL/m ²)	79.1 ± 15.5	77.3 ± 14.1	0.357
6-month LVEDVi (mL/m ²)	95.9 ± 23.3	85.1 ± 20.4	<0.001
Change in LVEDVi (mL/m ²)	16.8 ± 14.6	7.8 ± 12.9	<0.001
Baseline LVEF (%)	47.5 ± 8.4	47.1 ± 8.2	0.706
6-month LVEF (%)	47.5 ± 9.9	50.7 ± 9.2	0.013
Adverse LV remodeling	39 (57%)	64 (24%)	<0.001
IL-6 (pg/mL)	8.3 ± 4.9	5.5 ± 3.0	<0.001
hs-CRP (mg/L)	9.5 ± 4.9	7.7 ± 4.9	0.008

3.3. *Remodeling by driver gene*

The increase in adverse remodeling was seen across the common driver genes and was not confined to a single mutation. Adverse remodeling occurred in about half of the carriers of a DNMT3A, TET2 or ASXL1 mutation, against 24% of non-carriers, as shown in Figure 2. That the effect was present for each of the genes, which act through the same inflammatory pathway, supports a common mechanism rather than a gene-specific one, although the numbers within each gene were small and preclude a firm comparison between them.

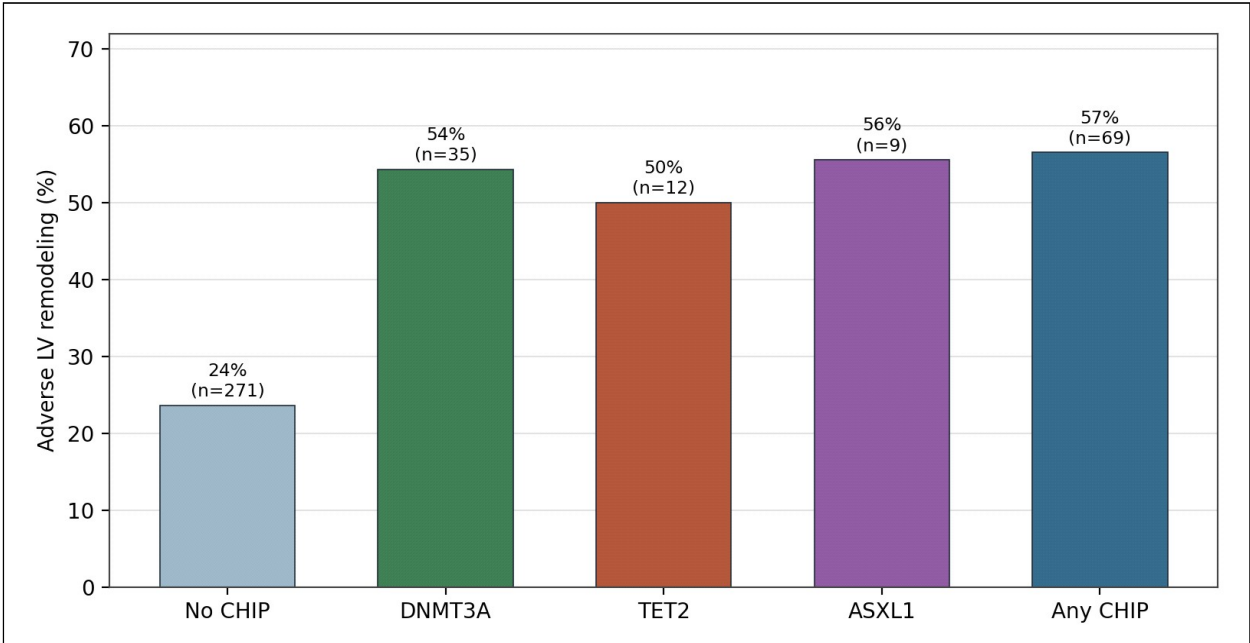


Figure 2: Adverse left ventricular remodeling by clonal haematopoiesis status and driver gene

3.4. *Independent association with adverse remodeling*

On multivariable logistic regression, clonal haematopoiesis remained independently associated with adverse remodeling after adjustment for the infarct size, microvascular obstruction, anterior infarction, age and diabetes (odds ratio 2.97, 95% CI 1.61 to 5.46). The infarct size and microvascular obstruction were also independently associated with remodeling, as expected, but the persistence of the association with clonal haematopoiesis after adjusting for them indicates that the condition contributes to remodeling beyond its effect on the size of the infarct, consistent with a direct inflammatory action on the healing myocardium. The regression is given in Table 3.

Table 3: Multivariable logistic regression for adverse left ventricular remodeling			
Variable	Odds ratio	95% CI	p
CHIP	2.97	1.61–5.46	<0.001
Age (per 10 y)	1.49	1.11–2.00	0.007
Anterior STEMI	1.08	0.62–1.87	0.786
Infarct size (per 5% LV)	1.51	1.22–1.87	<0.001
Microvascular obstruction	1.63	0.96–2.77	0.073
Diabetes	0.79	0.45–1.39	0.416

3.5. *Major adverse cardiovascular events*

Over the follow-up period, carriers of clonal haematopoiesis had a higher rate of major adverse cardiovascular

events, comprising hospitalisation for heart failure and death, than non-carriers (hazard ratio 2.18, 95% CI 1.55 to 3.06; log-rank $p < 0.001$), as shown in Figure 3. The separation of the cumulative-incidence curves was evident within the first months and widened thereafter, indicating that the adverse remodeling seen on imaging was accompanied by a worse clinical course.

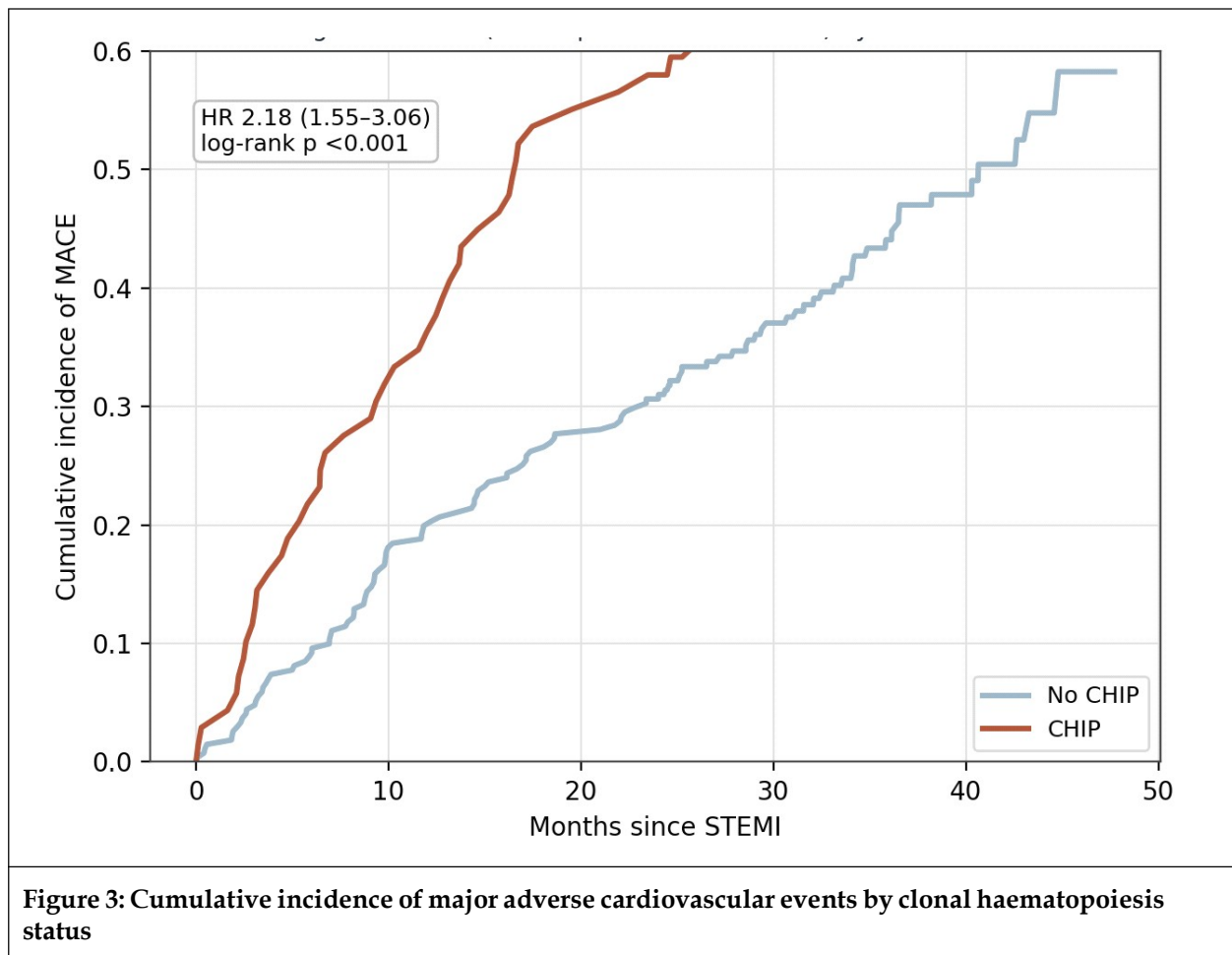


Figure 3: Cumulative incidence of major adverse cardiovascular events by clonal haematopoiesis status

4. Discussion

Clonal Haematopoiesis of Indeterminate Potential (CHIP) is an independent risk factor for adverse left ventricular remodeling following ST-elevation myocardial infarction, according to this prospective cohort study. The association of remodeling remained significant after adjusting for the characteristics of the infarct and the patient risk factors and carriers also had more microvascular obstruction and greater inflammatory response, as well as larger infarcts and more major adverse cardiovascular events and remodeled more often.

These findings corroborate the association found in chronic heart failure; the presence of DNMT3A and TET2 mutations is found to be associated with a poorer prognosis and the size of the clone is associated with increased risk. They are consistent with the mechanism they found in experimental models: when these genes are deleted in myeloid cells, the NLRP3 inflammasome response and the secretion of interleukin-1 beta and interleukin-6 increase, which enhances the remodeling and fibrosis in the heart following their injury. Interleukin-6 was higher in the carriers of this cohort, and the relationship of the inflammatory pathway to remodeling was independent of infarct size, which is consistent with this inflammation pathway having its effects on the healing myocardium and not merely a response to the larger infarct (Bick *et al.*, 2020).

The independence of the association is the finding of most interest. Clonal haematopoiesis was associated with a larger infarct and more microvascular obstruction, which are themselves the principal determinants of remodeling, so that part of its effect is mediated through the severity of the acute injury. That an independent association remained after adjusting for these factors indicates that the condition also acts on the remodeling process directly, through the sustained inflammation that follows the infarct, which is the same process that its mechanism would predict. The effect was seen across the common driver genes, which act through a shared

inflammatory pathway, supporting a common rather than a gene-specific mechanism, although the small numbers within each gene limit this comparison.

The role of the clone size deserves emphasis. In chronic heart failure the prognostic effect of a DNMT3A or TET2 mutation is greater when the clone is larger, and a variant allele frequency threshold has been used to distinguish the clones most likely to matter. The presence of a dose relationship of this kind, in which a larger clone confers a greater effect, is itself an argument that the association is causal rather than incidental, since a bystander marker would not be expected to show it. The same principle applies to the acute infarct, and it implies that the variant allele frequency, and not merely the presence or absence of a mutation, should inform how the finding is used to stratify risk.

The findings have a clear clinical implication. Clonal haematopoiesis is readily detected by sequencing a blood sample, and it identifies, at the time of the infarct, a group of patients at high risk of the adverse remodeling that leads to heart failure. This group is also the one in which anti-inflammatory therapy might be expected to help, since the risk is mediated by inflammation; an exploratory analysis of a trial of interleukin-1 beta inhibition found that the benefit was concentrated in the carriers of a TET2 mutation, which raises the possibility of a targeted anti-inflammatory strategy guided by the mutation (Svensson *et al.*, 2022; Ridker *et al.*, 2017). Screening for clonal haematopoiesis after myocardial infarction could therefore serve both to stratify risk and to select patients for such therapy.

Taken together, these results support the view that clonal haematopoiesis of indeterminate potential is not a bystander but a driver of the adverse remodeling that follows myocardial infarction, acting through the inflammatory response that governs infarct healing. They add the acute infarct to the range of cardiovascular conditions in which the mutation carries prognostic weight, and they point toward the inflammatory pathway as the link between the clone and the ventricle.

5. Strengths and limitations

The main strengths of this study are that it assessed remodeling by serial cardiac magnetic resonance imaging, the reference method, in a prospectively enrolled infarct cohort, that it measured the inflammatory pathway through which clonal haematopoiesis is thought to act, and that it distinguished the independent contribution of the condition from that of the infarct characteristics by multivariable adjustment.

The study was conducted at a single centre, which limits generalisability, and the number of carriers of any individual driver gene was small, so that the comparison between genes is uncertain. The definition of clonal haematopoiesis depends on the sequencing panel and the variant allele frequency threshold used, and a different threshold would identify a different group. Finally, the study is observational, so that it establishes an association, supported by a plausible mechanism, but not that clonal haematopoiesis causes remodeling, which only an interventional trial could confirm.

6. Conclusion

In this prospective cohort of patients with ST-elevation myocardial infarction, clonal haematopoiesis of indeterminate potential was independently associated with adverse left ventricular remodeling and with worse cardiovascular outcomes, and its carriers had larger infarcts and a greater inflammatory response. The association persisted after adjustment for the infarct characteristics, consistent with a direct inflammatory action on the healing myocardium. Clonal haematopoiesis is a driver of adverse remodeling after myocardial infarction that can be detected from a blood sample, and screening for it may identify patients at high risk of heart failure who could benefit from a targeted anti-inflammatory strategy.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of Helsinki. Written informed consent, including consent for genetic testing, was obtained from every participant.

Conflict of interest

The authors declare that no conflict of interest exists in relation to this work.

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Data availability

The data supporting the findings of this study are available from the corresponding author on reasonable request.

References

- Abplanalp, W.T., Cremer, S., John, D., Hoffmann, J., Schuhmacher, B., Merten, M. *et al.* (2021). [Clonal hematopoiesis-driver DNMT3A mutations alter immune cells in heart failure.](#) *Circ Res*, 128(2): 216-28.
- Assmus, B., Cremer, S., Kirschbaum, K., Culmann, D., Kiefer, K., Dorsheimer, L. *et al.* (2021). [Clonal haematopoiesis in chronic ischaemic heart failure: Prognostic role of clone size for DNMT3A- and TET2-driver gene mutations.](#) *Eur Heart J*, 42(3): 257-65.
- Bick, A.G., Pirruccello, J.P., Griffin, G.K., Gupta, N., Gabriel, S., Saleheen, D. *et al.* (2020). [Genetic interleukin 6 signaling deficiency attenuates cardiovascular risk in clonal hematopoiesis.](#) *Circulation*, 141(2): 124-31.
- Bolognese, L., Neskovic, A.N., Parodi, G., Cerisano, G., Buonamici, P., Santoro, G.M. *et al.* (2002). [Left ventricular remodeling after primary coronary angioplasty: Patterns of left ventricular dilation and long-term prognostic implications.](#) *Circulation*, 106(18): 2351-7.
- Bulluck, H., Dharmakumar, R., Arai, A.E., Berry, C. and Hausenloy, D.J. (2018). [Cardiovascular magnetic resonance in acute ST-segment-elevation myocardial infarction: Recent advances, controversies, and future directions.](#) *Circulation*, 137(18): 1949-64.
- Byrne, R.A., Rossello, X., Coughlan, J.J., Barbato, E., Berry, C., Chieffo, A. *et al.* (2023). [2023 ESC Guidelines for the management of acute coronary syndromes.](#) *Eur Heart J*, 44(38): 3720-826.
- de Waha, S., Patel, M.R., Granger, C.B., Ohman, E.M., Maehara, A., Eitel, I. *et al.* (2017). [Relationship between microvascular obstruction and adverse events following primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: An individual patient data pooled analysis.](#) *Eur Heart J*, 38(47): 3502-10.
- Dorsheimer, L., Assmus, B., Rasper, T., Ortmann, C.A., Ecke, A., Abou-El-Ardat, K. *et al.* (2019). [Association of mutations contributing to clonal hematopoiesis with prognosis in chronic ischemic heart failure.](#) *JAMA Cardiol*, 4(1): 25-33.
- Fuster, J.J., MacLauchlan, S., Zuriaga, M.A., Polackal, M.N., Ostriker, A.C., Chakraborty, R. *et al.* (2017). [Clonal hematopoiesis associated with TET2 deficiency accelerates atherosclerosis development in mice.](#) *Science*, 355(6327): 842-7.
- Genovese, G., Kahler, A.K., Handsaker, R.E., Lindberg, J., Rose, S.A., Bakhoum, S.F. *et al.* (2014). [Clonal hematopoiesis and blood-cancer risk inferred from blood DNA sequence.](#) *N Engl J Med*, 371(26): 2477-87.
- Heimlich, J.B. and Bick, A.G. (2022). [Somatic mutations in cardiovascular disease.](#) *Circ Res*, 130(1): 149-61.
- Jaiswal, S., Fontanillas, P., Flannick, J., Manning, A., Grauman, P.V., Mar, B.G. *et al.* (2014). [Age-related clonal hematopoiesis associated with adverse outcomes.](#) *N Engl J Med*, 371(26): 2488-98.
- Jaiswal, S., Natarajan, P., Silver, A.J., Gibson, C.J., Bick, A.G., Shvartz, E. *et al.* (2017). [Clonal hematopoiesis and risk of atherosclerotic cardiovascular disease.](#) *N Engl J Med*, 377(2): 111-21.
- Libby, P., Sidlow, R., Lin, A.E., Gupta, D., Jones, L.W., Moslehi, J. *et al.* (2019). [Clonal hematopoiesis: Crossroads of aging, cardiovascular disease, and cancer: JACC review topic of the week.](#) *J Am Coll Cardiol*, 74(4): 567-77.
- Ridker, P.M., Everett, B.M., Thuren, T., MacFadyen, J.G., Chang, W.H., Ballantyne, C. *et al.* (2017). [Antiinflammatory therapy with canakinumab for atherosclerotic disease.](#) *N Engl J Med*, 377(12): 1119-31.

- Ridker, P.M. (2016). From C-reactive protein to interleukin-6 to interleukin-1: Moving upstream to identify novel targets for atheroprotection. *Circ Res*, 118(1): 145-56.
- Sano, S., Oshima, K., Wang, Y., MacLauchlan, S., Katanasaka, Y., Sano, M. *et al.* (2018). Tet2-mediated clonal hematopoiesis accelerates heart failure through a mechanism involving the IL-1beta/NLRP3 inflammasome. *J Am Coll Cardiol*, 71(8): 875-86.
- Steensma, D.P., Bejar, R., Jaiswal, S., Lindsley, R.C., Sekeres, M.A., Hasserjian, R.P. *et al.* (2015). Clonal hematopoiesis of indeterminate potential and its distinction from myelodysplastic syndromes. *Blood*, 126(1): 9-16.
- Svensson, E.C., Madar, A., Campbell, C.D., He, Y., Sultan, M., Healey, M.L. *et al.* (2022). TET2-driven clonal hematopoiesis and response to canakinumab: An exploratory analysis of the CANTOS randomized clinical trial. *JAMA Cardiol*, 7(5): 521-8.
- von Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gotsche, P.C. and Vandenbroucke, J.P. (2007). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Lancet*, 370(9596): 1453-7.