# High-Dose Allopurinol Reduces Left Ventricular Mass in Patients With Ischemic Heart Disease

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**Objectives**      This study sought to ascertain if high-dose allopurinol regresses left ventricular mass (LVM) in patients with ischemic heart disease (IHD).

**Background**      LV hypertrophy (LVH) is common in patients with IHD including normotensive patients. Allopurinol, a xanthine oxidase inhibitor, has been shown to reduce LV afterload in IHD and may therefore also regress LVH.

**Methods**      A randomized, double-blind, placebo-controlled, parallel group study was conducted in 66 patients with IHD and LVH, comparing 600 mg/day allopurinol versus placebo therapy for 9 months. The primary outcome measure was change in LVM, assessed by cardiac magnetic resonance imaging (CMR). Secondary outcome measures were changes in LV volumes by CMR, changes in endothelial function by flow-mediated dilation (FMD), and arterial stiffness by applanation tonometry.

**Results**      Compared to placebo, allopurinol significantly reduced LVM (allopurinol $-5.2 \pm 5.8$ g vs. placebo $-1.3 \pm 4.48$ g; p = 0.007) and LVM index (LVMI) (allopurinol $-2.2 \pm 2.78$ g/m$^2$ vs. placebo $-0.53 \pm 2.5$ g/m$^2$; p = 0.023). The absolute mean difference between groups for change in LVM and LVMI was $-3.89$ g (95% confidence interval: $-1.1$ to $-6.7$) and $-1.67$ g/m$^2$ (95% confidence interval: $-0.23$ to $-3.1$), respectively. Allopurinol also reduced LV end-systolic volume (allopurinol $-2.81 \pm 7.8$ mls vs. placebo $+1.3 \pm 7.22$ mls; p = 0.047), improved FMD (allopurinol $+0.82 \pm 1.8\%$ vs. placebo $-0.69 \pm 2.8\%$; p = 0.017) and augmentation index (allopurinol $-2.8 \pm 5.1\%$ vs. placebo $+0.9 \pm 7\%$; p = 0.02).

**Conclusions**      High-dose allopurinol regresses LVH, reduces LV end-systolic volume, and improves endothelial function in patients with IHD and LVH. This raises the possibility that allopurinol might reduce future cardiovascular events and mortality in these patients. (Does a Drug Allopurinol Reduce Heart Muscle Mass and Improve Blood Vessel Function in Patients With Normal Blood Pressure and Stable Angina?; ISRCTN73579730)      (J Am Coll Cardiol 2013; 61:926–32) © 2013 by the American College of Cardiology Foundation

Cardiovascular disease is the most common cause of death in the western world. Most of the attention in treating ischemic heart disease (IHD) is understandably directed toward treating coronary artery disease. However there are other treatable culprits in these patients.

Left ventricular hypertrophy (LVH) is widespread in IHD patients, even in the absence of hypertension (1). It is

a strong predictor of cardiovascular events and all-cause mortality (2). In one study, the presence of LVH was a stronger predictor of mortality than either multivessel coronary disease or impaired LV function (3). The reason why LVH is so adverse is because it predates many different cardiovascular events (i.e., LVH is arrhythmogenic and causes sudden death, impedes LV filling and leads to diastolic heart failure, reduces coronary perfusion reserve, and causes left atrial enlargement, atrial fibrillation, and

cardioembolic strokes) (4). Regression of LVH has been associated with an improved prognosis, independent of change in blood pressure (BP) (5–7). Therefore, cardiovascular events and mortality in IHD might well be reduced if we can find novel therapies to regress LVH.

Allopurinol, a xanthine oxidase inhibitor, may regress left ventricular mass (LVM) in IHD patients for a number of reasons. First, xanthine oxidase inhibitors have been shown to regress LVM in several animal models (8–10). Second, a recent human study has shown allopurinol to regress LVM in chronic kidney disease patients (11). Third, allopurinol may also regress LVM because it reduces augmentation index in patients with IHD, thereby reducing LV afterload (12).

Hence, the main aim of this study was to assess whether allopurinol could regress LVM in patients on optimal, current evidence-based therapy for IHD. The secondary aim was to assess the effect of allopurinol on LV volumes, endothelial function, and arterial stiffness in this patient group.

## Methods

**Study overview.** This was a randomized, double-blind, placebo controlled, parallel group study using a 9-month treatment period at a single center in Dundee, Scotland. It was approved by the Tayside Research Ethics Committee and was done in accordance with the Declaration of Helsinki. All patients provided written informed consent. This study has been registered with the International Standard Randomized Controlled Trial Number register ISRCTN73579730.

**Study participants.** Sixty-six adult patients were recruited from hospital cardiology databases and local general practices. They had to have either angiographically documented coronary artery disease (80%) or a previous history of myocardial infarction (12%), or both typical symptoms of angina and a positive stress test for ischemia (8%). In the latter group, the stress test was an exercise tolerance test in 3 patients and a nuclear myocardial perfusion scan in 2 patients. They were also required to have an office BP <150/90 mm Hg and the presence of LVH on echocardiography (American Society of Echocardiography criteria LVM index [LVMI] >115 $g/m^2$ for men and >95 $g/m^2$ for women) (13). Patients were excluded if they were currently prescribed allopurinol or azathioprine, had a previous adverse reaction to allopurinol, or active gout. They were also excluded if they had renal dysfunction (glomerular filtration rate < 60 ml/min), heart failure, or malignancy, or were unable to give informed consent. Patients with contraindications to cardiac magnetic resonance (CMR) (pacemakers, claustrophobia) were also excluded, as were pregnant or lactating women.

**Randomization and masking.** Baseline assessments and investigations (blood tests, flow-mediated dilation [FMD] of the brachial artery in response to hyperemia, applanation tonometry, CMR) were performed followed by randomization by a computer-generated random allocation sequence. Patients were randomly assigned to receive either allopurinol 100 mg/day or placebo for 2 weeks. If this was tolerated, the trial medication dosage was increased to allopurinol 300 mg/day for a month. After 1 month of treatment, the dosage was increased to 300 mg twice daily of allopurinol or placebo therapy for a further 7.5 months. Blood tests were taken at baseline and final visit for full blood count, renal function, liver function, uric acid, B-type natriuretic peptide (BNP) and oxidized low-density lipoprotein. Office BP was measured for all the patients at each visit (2, 6, 10, 28, and 39 weeks) by the same blinded investigator after the subject had rested for at least 10 min. Furthermore, 32 randomly selected patients had a 24-h BP ambulatory monitor at baseline and final visit. During the study, all patients continued their concomitant medication.

**Cardiac magnetic resonance imaging.** Cardiac magnetic resonance imaging was performed at baseline and at 9 months on a 3T Magnetom Trio scanner (Siemens, Erlangen, Germany) using body array and spine matrix radiofrequency coils as described in detail by us previously (11). CMR images were analyzed offline by an independent, blinded magnetic resonance imaging (MRI) physicist (S.J.G.) using commercial software (Argus, Siemens Multi-modality Work Platform, version VB 15, Siemens of Erlangen, Germany). Electronic region of interest contours were placed around endocardial and epicardial LV borders on all CMR image slices at end-diastole and end-systole that were identified to contain 50% or more full-thickness myocardium. Papillary muscles were included in the LVM if the muscle structure was indistinguishable from the myocardial wall, but otherwise assigned to the LV blood pool. The process of contour placement was repeated such that every patient dataset at both time points was analyzed twice in order to optimize the measurement precision.

**FMD.** Endothelial function was assessed by measuring FMD of the brachial artery in response to hyperemia as set out in the International Brachial Artery Reactivity Task Force guidelines and as performed regularly at our institute (12,14,15). FMD was performed at the baseline visit, 6 months, and 9 months using a Sequoia 512 (Siemens, Camberley, England) ultrasound machine with a 8 MHz linear array probe. The FMD was analyzed using Vascular Research Tools software (Medical Imaging Applications LLC, Coralville, Iowa). The acquisition and analyses of the FMD images were performed by a single trained investigator (S.R.), who was blinded to the allocated treatment.

**Applanation tonometry.** Pulse wave analysis and pulse wave velocity (PWV) were measured at baseline, 6 months visit, and 9 months visit using the validated Sphygmocor (AtCor, Sydney, Australia) system by a single trained investigator (S.R.) who was blinded to the allocated treatment. This technique is in widespread use in our institute
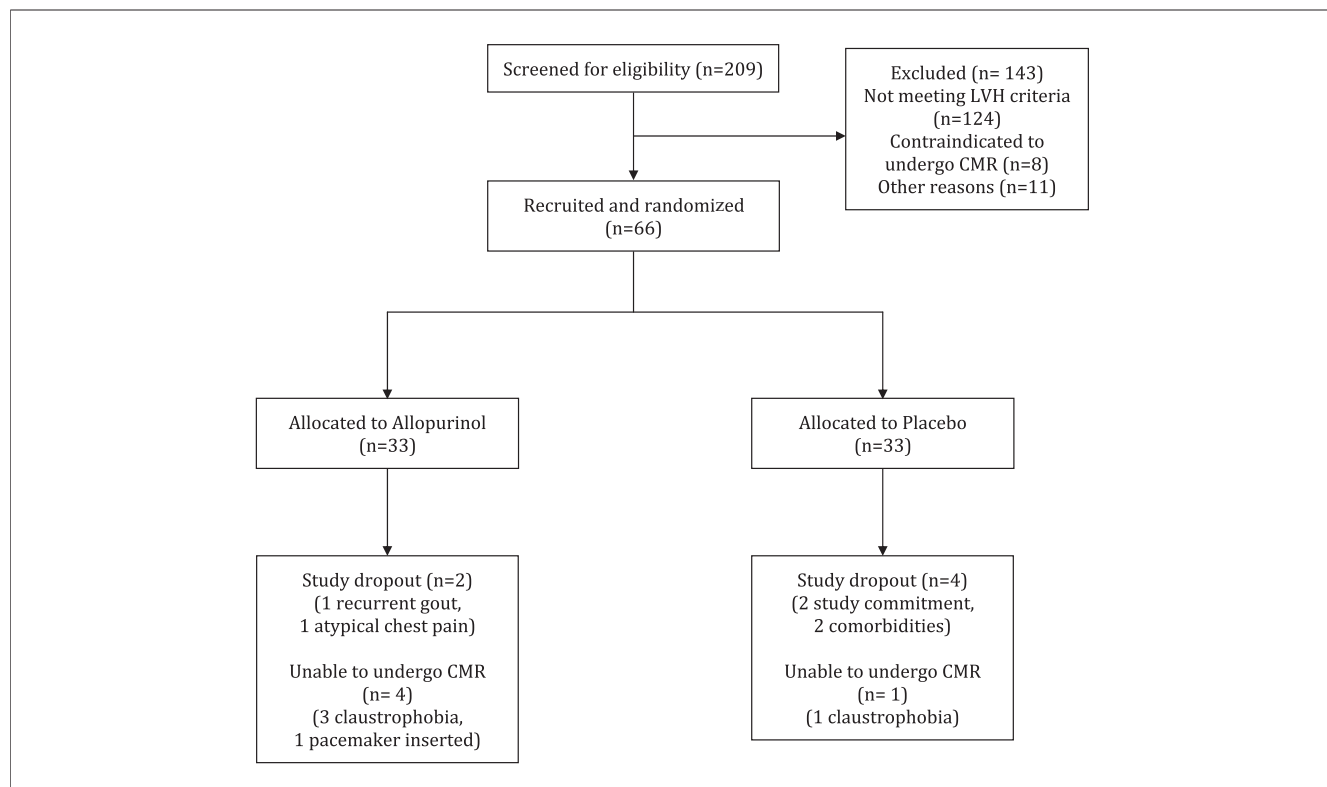
**Figure 1    Flow Diagram of the Study**

CMR = cardiac magnetic resonance; LVH = left ventricular hypertrophy.

and our methodology was as described subsequently (12). From the aortic pulse wave, augmentation index (AIx) was calculated as the difference between the first and second systolic peak expressed as a percentage of the pulse pressure. As AIx is affected by heart rate, AIx was normalized for a heart rate of 75 beats/min. For PWV, radial-carotid waveforms were obtained with electrocardiogram gating.

**Statistical analysis.** The primary endpoint was LVM on CMR. We followed the recommendations of Grothues et al. (16), which advised that 30 patients would be needed to detect a 10-g change in LVM at 90% power, on the basis of a reproducibility figure of 3.6%. In fact, we doubled our numbers to 60 patients and then to 66 patients to account for 10% dropouts. We doubled our numbers because we thought 30 patients was a bit tight and because it would be challenging to regress LVM by 10 g in only 9 months with no expected change in BP. Using Grothues et al. reproducibility figure, our 60 patients study had 90% power to detect a 5-g change in LVM. We were also aware that this figure matched the differential change in LVMI between the treatments in the echo substudy of the LIFE (Losartan Intervention For Endpoint reduction in hypertension) study (7).

Data for continuous variables are presented as mean ± SD for normally distributed data and median and interquartile range for non-normally distributed data. Categorical data are expressed as numbers (%). Comparisons between continuous variables were analyzed using the Student *t* test

or Mann-Whitney *U* test while categorical variables were analyzed using chi-square test. Correlation was performed using Pearson's or Spearman's method.

All statistical analyses were undertaken using SPSS version 18.0 (SPSS, Chicago, Illinois). A 2-sided p value <0.05 was considered statistically significant.

## Results

A total of 66 patients were recruited for this study. Only 1 patient had ever before received allopurinol (27 months earlier). As there were 6 study dropouts (allopurinol n = 2, placebo n = 4), 60 underwent FMD and applanation tonometry while 55 patients completed CMR (Fig. 1, Table 1).

Treatment with high-dose allopurinol significantly reduced LVM (change in LVM: allopurinol group −5.2 ± 5.8 g vs. placebo group −1.3 ± 4.48 g; p = 0.007) and LVMI (change in LVMI: allopurinol group −2.2 ± 2.78 g/m² vs. placebo group −0.53 ± 2.5 g/m²; p = 0.023) (Fig. 2). The absolute mean difference between the groups for change in LVM was −3.89 g (95% confidence interval: −1.1 to −6.7) and −1.67 g/m² (95% confidence interval: −0.23 to −3.1) for change in LVMI. The change in LVM in the allopurinol group remained statistically significant even after correcting for baseline LVM (p= 0.013). Furthermore, the within-group changes in LVM and LVMI were significant in the allopurinol group (p < 0.001 for

| Table 1 | Baseline Characteristics of Study Participants | | |
| --- | --- | --- | --- |
| | Allopurinol (n = 31) | Placebo (n = 29) | p Value |
| Age, yrs | 65 ± 6.7 | 64 ± 7.2 | 0.64 |
| Male | 26 (84%) | 28 (97%) | 0.1 |
| BSA, g/m$^2$ | 2.05 ± 0.18 | 2.0 ± 0.2 | 0.26 |
| Office SBP, mm Hg | 135 ± 9 | 134 ± 10 | 0.87 |
| 24-h SBP, mm Hg | 124 ± 11 | 121 ± 9 | 0.42 |
| Office DBP, mm Hg | 78 ± 6.8 | 76 ± 7 | 0.26 |
| 24-h DBP, mm Hg | 70 ± 5 | 74 ± 5 | 0.06 |
| Past MI | 13 (42%) | 17 (59%) | 0.2 |
| Hypertension | 23 (74%) | 16 (55%) | 0.12 |
| Diabetes | 4 (13%) | 3 (10%) | 0.8 |
| Cerebrovascular disease | 4 (13%) | 2 (7%) | 0.4 |
| Peripheral vascular disease | 3 (9.7%) | 2 (7%) | 0.7 |
| Smoking | | | 0.24 |
| Non | 7 (22.6%) | 12 (41%) | |
| Ex | 19 (61.3%) | 12 (41%) | |
| Current | 5 (16.1%) | 5 (17%) | |
| CCS classification | | | 0.88 |
| 1 | 23 (74%) | 21 (72%) | |
| 2 | 8 (26%) | 8 (28%) | |
| Positive stress test in those without angiogram/ previous MI | 3 (9.7%) | 2 (6.9%) | 0.17 |
| No. of vessel disease | | | 0.047 |
| 1 | 2 (7%) | 12 (41%) | |
| 2 | 11 (36%) | 8 (28%) | |
| 3 | 9 (29%) | 6 (21%) | |
| PCI | 6 (19%) | 15 (52%) | 0.01 |
| CABG | 15 (48%) | 8 (28%) | 0.1 |
| Aspirin | 26 (83.9%) | 29 (100%) | 0.024 |
| Clopidogrel | 4 (12.9%) | 4 (14%) | 0.94 |
| Statin | 29 (93.5%) | 27 (93%) | 0.916 |
| Ezetimibe | 3 (9.7%) | 2 (7%) | 0.7 |
| Beta-blocker | 24 (77.4%) | 18 (62%) | 0.2 |
| Calcium-channel blocker | 10 (32.3%) | 13 (45%) | 0.3 |
| Nicorandil | 2 (6.5%) | 6 (21%) | 0.1 |
| Isosorbide mononitrate | 9 (29%) | 11 (38%) | 0.47 |
| ACE inhibitor | 20 (64.5%) | 15 (52%) | 0.32 |
| ARB | 7 (22.6%) | 3 (10%) | 0.2 |
| Uric acid, mmol/l | 0.59 ± 0.09 | 0.56 ± 0.14 | 0.326 |
| BNP, pg/ml | 31.0 (21–60) | 20.6 (13–35) | 0.026 |
| FMD | 4.1 ± 2.1 | 5.68 ± 2.4 | 0.01 |
| AIx | 20 ± 7 | 19.5 ± 9 | 0.73 |
| PWV, m/s | 7.6 (6.9 to 8.7) | 8.5 (7.4 to 9) | 0.022 |
| CMR LVM, g | 145.7 ± 23.4 | 136.4 ± 26 | 0.17 |
| CMR LVMI, g/m$^2$ | 70.98 ± 9 | 68.39 ± 11.14 | 0.347 |

Values are mean ± SD, n (%), or median (interquartile range).

ACE inhibitor = angiotensin-converting enzyme inhibitor; AIx = augmentation index; ARB = angiotensin receptor blocker; BNP = B-type natriuretic peptide; BSA = body surface area; CABG = coronary artery bypass grafting; CCS = Canadian Cardiovascular Society; CMR = cardiac magnetic resonance; DBP = diastolic blood pressure; FMD = flow mediated dilation; LVM = left ventricular mass; LVMI = left ventricular mass index; MI = myocardial infarction; PCI = percutaneous coronary intervention; PWV = pulse wave velocity; SBP = systolic blood pressure.



**Figure 2    Effect of Allopurinol on Change in LVMI and LVM**

**(A)** This graph illustrates the effect of 9 months of allopurinol or placebo treatment on the change in LVMI. Allopurinol significantly reduced LVMI after 9 months of therapy compared with placebo (p = 0.023). Data are expressed as mean ± SEM. **(B)** This graph illustrates the effect of 9 months of allopurinol or placebo treatment on the change in LVM. Allopurinol significantly reduced LVM after 9 months of therapy compared with placebo (p = 0.007). Data are expressed as mean ± SEM.

Allopurinol also significantly reduced LV end-systolic volume (allopurinol group −2.81 ± 7.8 mls vs. placebo group +1.3 ± 7.22 mls; p = 0.047) and nonsignificantly reduced LV end-diastolic volume (allopurinol group −6.05 ± 16.42 mls vs. placebo group +0.48 ± 16.87 mls; p = 0.15) (Table 2). Allopurinol was associated with a reduction in median BNP just short of statistical significance (allopurinol

| Table 2 | CMR Changes Seen After Allopurinol Treatment | | |
| --- | --- | --- | --- |
| | Allopurinol (n = 27) | Placebo (n = 28) | p Value |
| Change in LVM, g | −5.2 ± 5.8 | −1.3 ± 4.48 | 0.007 |
| Change in LVMI, g/m$^2$ | −2.2 ± 2.78 | −0.53 ± 2.5 | 0.023 |
| % change in LVM | −3.57 ± 3.98 | −0.98 ± 3.29 | 0.01 |
| % change in LVMI | −3.29 ± 4.29 | −0.85 ± 3.7 | 0.028 |
| Change in EF, % | 0.58 ± 3.27 | −0.61 ± 3.71 | 0.24 |
| Change in EDV, mls | −6.05 ± 16.42 | 0.48 ± 16.87 | 0.15 |
| Change in ESV, mls | −2.81 ± 7.8 | 1.3 ± 7.22 | 0.047 |
| Change in SV, mls | −3.28 ± 12.78 | −0.81 ± 13.25 | 0.49 |
| Change in CO, l/min | −0.085 ± 0.93 | 0.11 ± 0.89 | 0.44 |

Values are mean ± SD.

CO = cardiac output; EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; SV = stroke volume; other abbreviations as in Table 1.

both) but not in the placebo group (Table 2). We found no significant differences in the allopurinol-induced change in either LVM or LVMI (p = 0.15 and p = 0.25, respectively) between those with a past history of MI versus those without a past history of MI.
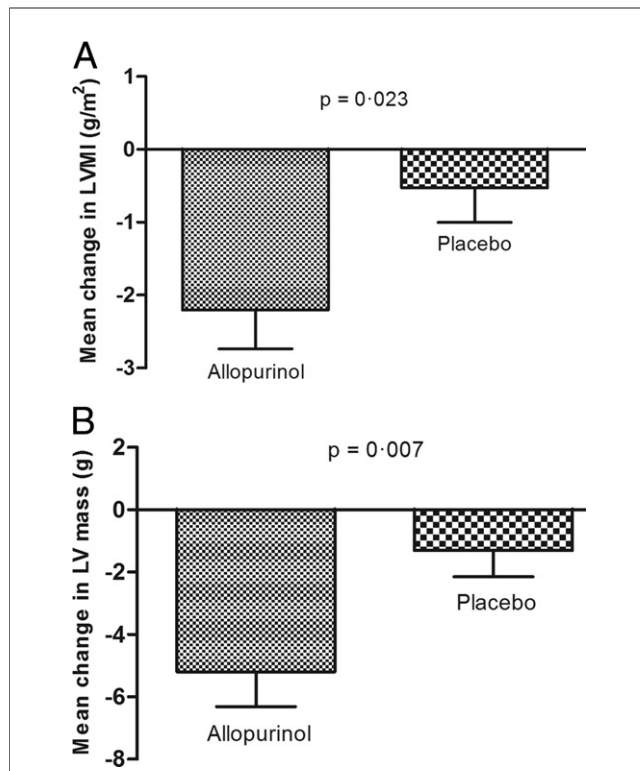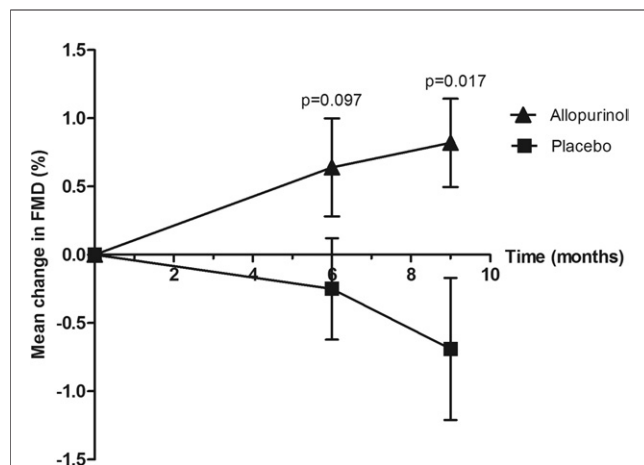
**Figure 3    Effect of Allopurinol on the Change in FMD**

This graph illustrates the effect of 6 months and 9 months of allopurinol **(triangles)** or placebo **(squares)** treatment on the change in flow-mediated dilation (FMD). Allopurinol significantly improved FMD after 9 months of therapy compared with placebo (p = 0.017). Data are expressed as mean ± SEM.



**Figure 4    Effect of Allopurinol on the Change in AIx**

This graph illustrates the effect of 6 months and 9 months of allopurinol **(triangles)** or placebo **(squares)** treatment on the change in augmentation index (AIx). Allopurinol significantly improved AIx after 9 months of therapy compared with placebo (p = 0.02). Data are expressed as mean ± SEM.

group −5.5 pg/ml [−19 to 5 pg/ml], placebo group −1.1 pg/ml [−7 to 5 pg/ml]; p = 0.08).

At baseline, brachial artery size was similar between the groups but there was a significant difference in baseline FMD (allopurinol group 4.1 ± 2.1% vs. placebo group 5.68 ± 2.4%; p = 0.01). However, allopurinol improved FMD, which was significant at 9 months (change in FMD allopurinol group: 0.82 ± 1.8% vs. placebo −0.69 ± 2.8%; p = 0.017) (Fig. 3, Table 3). Within the allopurinol group, FMD changes were also significant (p = 0.019), whereas this was not the case in the placebo group. Interestingly, allopurinol significantly reduced the response to GTN compared to placebo, which agrees with some recent data but not with others (12,17). Allopurinol also significantly reduced AIx, which was statistically significant at 9 months. Within the allopurinol group itself, AIx changes were
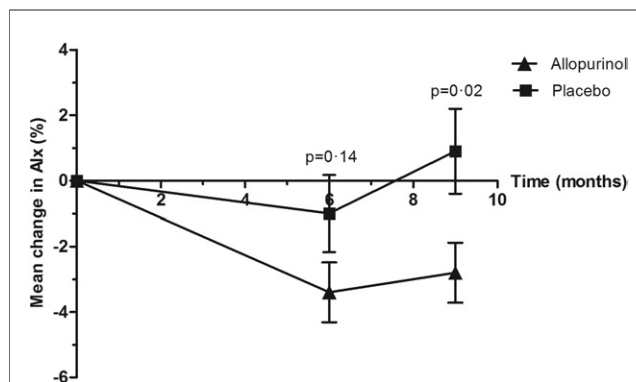
significant (p = 0.004), while this was not the case within the placebo group (Table 3, Fig. 4).

Allopurinol did not have any significant effect on office BP or 24-h ambulatory BP (Table 3). Allopurinol reduced uric acid by 46% from 0.59 ± 0.09 mmol/l to 0.32 ± 0.1 mmol/l after 9 months of treatment. No correlation was seen between the change in LVM and the change in FMD, AIx, PWV, or uric acid. All patients tolerated a daily dosage of 600 mg of allopurinol except 1 patient who was left on 300 mg as she developed a rash while taking 600 mg.

## Discussion

The main finding of this study is that high-dose allopurinol reduces LVM in patients with IHD and LVH who are on current evidence-based optimal therapy. The secondary findings are that high-dose allopurinol reduces LV end-systolic volume and improves endothelial function and arterial stiffness.

**Table 3    Effect of Allopurinol on Hemodynamics and Endothelial Function**

| | Allopurinol (n = 31) | Placebo (n = 29) | p Value |
|---|---|---|---|
| Change in office SBP, mm Hg | −5 ± 13 | −3 ± 15 | 0.59 |
| Change in office DBP, mm Hg | −4.2 ± 8.0 | −1.4 ± 8.0 | 0.2 |
| Change in 24-h SBP, mm Hg | 1.5 ± 11.0 | −3.6 ± 8.5 | 0.17 |
| Change in 24-h DBP, mm Hg | 0.76 ± 5.0 | −2.6 ± 4.0 | 0.61 |
| Change in FMD response to hyperemia at 6 months, % | 0.64 ± 2.0 | −0.25 ± 2.0 | 0.097 |
| Change in FMD response to hyperemia at 9 months, % | 0.82 ± 1.8 | −0.69 ± 2.8 | 0.017 |
| Change in response to GTN at 6 months, % | −0.96 ± 3.0 | 0.8 ± 3.1 | 0.036 |
| Change in response to GTN at 9 months, % | −1.4 ± 2.8 | 1.1 ± 3.3 | 0.002 |
| Change in AIx at 6 months, % | −3.4 ± 5.1 | −1.0 ± 6.3 | 0.14 |
| Change in AIx at 9 months, % | −2.8 ± 5.1 | 0.9 ± 7.0 | 0.02 |
| Change in PWV at 6 months, m/s | 0 (−0.6 to 0.3) | 0 (−0.78 to 0.4) | 0.85 |
| Change in PWV at 9 months, m/s | −0.14 (−0.8 to 0.3) | −0.2 (−1.25 to 0.4) | 0.66 |

Values are mean ± SD or median (interquartile range).
Abbreviations as in Table 1.

The regression of LVH with allopurinol therapy seen in this study is consistent with a recently published human study showing that allopurinol regresses LVM in chronic kidney disease (11). It is also consistent with 3 experimental animal studies showing that xanthine oxidase inhibitors can regress LVH (8–10). Our secondary findings are consistent with a recently published study showing allopurinol to improve FMD and AIx in very similar patients (12).

LVH is one of the most reliable surrogate markers we have in cardiovascular medicine (18,19). In fact, the LIFE study has shown that LVH regression per se can be associated with reduced all-cause mortality (by 28%), cardiovascular mortality (by 38%), sudden cardiac death (by 19%), myocardial infarction (by 15%), new congestive heart failure (by 36%), new onset atrial fibrillation (by 12%), and stroke (by 24%), and that these are all independent of any change in BP (20–22). It remains to be seen whether allopurinol-induced LVH regression can deliver anything similar to these effects that were seen in the LIFE study.

What is the mechanism by which allopurinol regresses LVM? One possibility could be that allopurinol reduces oxidative stress which then regresses LVH (12,15,23). However, in this study, allopurinol did not change oxidized low-density lipoprotein levels. The second possible mechanism is that allopurinol causes a significant reduction in AIx and improved endothelial function without a significant effect on BP suggesting improved arterial compliance, which should also reduce cardiac afterload. A reduction in AIx has been shown to be the best predictor of LVM regression and this is the third study to show that allopurinol reduces AIx (11,12,24). An effect on LV afterload is supported by our significant reduction in end-systolic volume and nonsignificant reductions in both end-diastolic volume and BNP. Although allopurinol had no effect on BP in this and in other studies, this study was not powered to detect an effect on BP as such and it remains possible that some of the LVH regression seen here was due to subtle changes in BP (12,15).

This new effect of allopurinol therapy on LVM regression in patients with IHD is on top of a recently documented anti-ischemic effect of allopurinol in angina patients (25). The prospect of allopurinol reducing cardiovascular events is enhanced by it having this dual effect of being both anti-ischemic and reducing LVH. It is further enhanced by data in this study showing that allopurinol improves vascular function (FMD, AIx), reduces end-systolic volume, and nearly reduces BNP. It is really this collection of favorable changes in key surrogates that makes the case that allopurinol might reduce cardiovascular events. Indeed, 2 other small randomized controlled trials show this already (26,27).

We chose to prescribe allopurinol at a dosage of 600 mg/day as a previous study showed a strong dose-response curve with a greater improved endothelial function with 600 mg/day compared to 300 mg/day (15). According to the British National Formulary, allopurinol can be given up to a dosage of 900 mg/day in the treatment of gout in patients with normal renal function although doses of 100 to 300 mg/day are most commonly prescribed in clinical practice. **Study limitations.** This is a single-center study with a relatively small number of patients. It is almost inevitable with so many demographic parameters that a few will by chance be different at baseline, although few differences were statistically significant. Additionally, the patients recruited in this study were predominantly men and the number of diabetic patients was low. Finally, although significant, the effect of allopurinol on LVM is modest, although it is similar in percentage terms to what was seen between the 2 treatments in the echo substudy of the LIFE trial (7).

## Conclusions

Allopurinol reduces LVM in patients with IHD and LVH. It also improves vascular function, LV afterload, and LV end-systolic volume. This work increases the prospect that allopurinol might reduce cardiovascular events or mortality in patients with IHD. A large multicenter randomized controlled trial is now indicated.

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**Key Words:** allopurinol ■ ischemic heart disease ■ oxidative stress ■ ventricular hypertrophy.