

septal reduction therapies in surgical candidates. In fact, this issue is the objective of the ongoing VALOR-HCM trial (NCT04349072). However, in a broad perspective, surgical myectomy and alcohol septal ablation should not be considered a panacea for patients with hypertrophic cardiomyopathy, and ideal results are far from guaranteed outside a limited number of centres that have experienced high patient volumes.^{3,4} Therefore, effective medical therapies such as mavacamten might be particularly important as an alternative in many settings.

From the patients' perspective, the possibility to have surgical results without surgery is highly desirable. It is no surprise that there is enthusiasm for a first-in-class disease-targeted therapy supported by robust evidence in this pivotal trial. Further studies are now ongoing to establish how to best position this novel treatment among available options for our patients.

DJ has received personal fees from MyoKardia. CYH has received payments as a consultant from MyoKardia and Ambry Genetics. SJL has received payments as a consultant from MyoKardia. AW has received grants from MyoKardia; personal fees from Cytokinetics; and payments as a consultant from MyoKardia. IO has received grants from MyoKardia, Sanofi-Genzyme, Shire, and Bayer; personal fees from Sanofi-Genzyme, Shire, and Bayer; and payments as a consultant from MyoKardia.

*Daniel Jacoby, Carolyn Y Ho,
Steven J Lester, Andrew Wang,
Jacopo Olivotto
iacopo.olivotto@unifi.it

Department of Internal Medicine, Section of Cardiovascular Medicine, Yale University, New Haven, CT, USA (DJ); Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston, MA, USA (CYH); Department of Cardiovascular Diseases, Mayo Clinic Arizona, Phoenix, AZ, USA (SJL); Duke University School of Medicine, Durham, NC, USA (AW); Cardiomyopathy Unit, Azienda Ospedaliera Universitaria Careggi, Florence 50134, Italy (IO); Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy (IO)

- Olivotto I, Oreziak A, Barriales-Villa R, et al. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2020; **396**: 759–69.
- Smith JR, Layrissa V, Medina-Inojosa JR, et al. Predictors of exercise capacity following septal myectomy in patients with hypertrophic cardiomyopathy. *Eur J Prev Cardiol* 2020; **27**: 1066–73.

- Maron BJ, Yacoub M, Dearani JA. Controversies in cardiovascular medicine. Benefits of surgery in obstructive hypertrophic cardiomyopathy: bring septal myectomy back for European patients. *Eur Heart J* 2011; **32**: 1055–58.
- Kim LK, Swaminathan RV, Looser P, et al. Hospital volume outcomes after septal myectomy and alcohol septal ablation for treatment of obstructive hypertrophic cardiomyopathy. *JAMA Cardiol* 2016; **1**: 324–32.

Managing NSTEMI in older patients

In the SENIOR-NSTEMI study, Amit Kaura and colleagues¹ exploit state-of-the-art statistical approaches including target trial design, propensity score-adjusted regression, and inverse probability of treatment weighting, with the results clearly favouring an invasive management strategy in older patients (≥ 80 years old) with NSTEMI. However, some additional details should be provided by the investigators, to avoid any suspicion of residual confounding factors and strengthen the evidence that the invasive strategy is actually and mechanistically beneficial. Invasive management entails an invasive coronary angiography early on during treatment, and only the accurate reporting and analysis of diagnostic findings and ensuing treatments can confirm that there has not been a so-called black-box effect.²

In particular, focusing on diagnostic features, no details were provided on the extent and severity of coronary artery disease (eg, location and number of coronary stenoses), despite their notable prognostic effect and influence on the management strategy.³ Although revascularisation was done in 74% of patients undergoing invasive management, no additional details on the type of revascularisation are provided. Moreover, no details on subsequent ancillary medical therapy (including, but not limited to, antithrombotic therapy) are given. On a potentially smaller note, 4% of patients were excluded because of missing data. This approach risks creating systematic bias, and we would also recommend a sensitivity analysis based on missing

data imputation and subsequent pooling, according to the Rubin rule.⁴

Although we find the SENIOR-NSTEMI trial and its findings useful, their effect and credibility would definitely be strengthened by providing additional details and analyses.

GB-Z has consulted for Cardionovum, InnovHeart, Meditrial, and Replycare. All other authors declare no competing interests.

*Francesco Versaci, Giacomo Frati,
Giuseppe Biondi-Zoccai
giuseppe.biondizoccai@uniroma1.it

Unità Operativa Complessa di Unità di Terapia Intensiva Coronarica, Emodinamica e Cardiologia, Ospedale S Maria Goretti, Latina, Italy (FV); Department of Medical-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina 04100, Italy (GF, GB-Z); IRCCS NEUROMED, Pozzilli, Italy (GF); Mediterranea Cardiocentro, Napoli, Italy (GB-Z)

- Kaura A, Sterne JAC, Trickey A, et al. Invasive versus non-invasive management of older patients with non-ST elevation myocardial infarction (SENIOR-NSTEMI): a cohort study based on routine clinical data. *Lancet* 2020; **396**: 623–34.
- Leeming J. The "black box" effect in science communication. Nov 4, 2016. <http://blogs.nature.com/naturejobs/2016/11/04/the-black-box-effect-in-science-communication/> (accessed Nov 12, 2020).
- Stepien K, Nowak K, Skorek P, et al. Baseline indicators of coronary artery disease burden in patients with non-ST-segment elevation acute coronary syndrome. *Minerva Cardioangiol* 2019; **67**: 181–90.
- Granger E, Sergeant JC, Lunt M. Avoiding pitfalls when combining multiple imputation and propensity scores. *Stat Med* 2019; **38**: 5120–32.

With the results of the SENIOR-NSTEMI study, Amit Kaura and colleagues¹ conclude that invasive management reduced 3-year mortality by 36% and hospital admissions for heart failure by 33%. These are illustrative results, but some aspects need further discussion.

First, Kaura and colleagues did not analyse or adjust for heart failure incidence during the index acute coronary syndrome, which we have shown to have a crucial effect on mortality and post-discharge heart failure.²

Second, Kaura and colleagues did not do a competing event regression analysis, and their analyses might overestimate the effect. The competing risk regression was developed for situations when the