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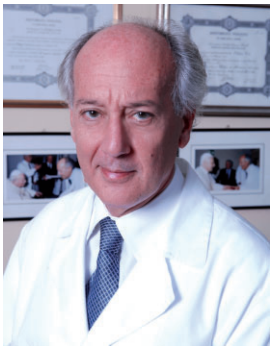
ISSUE @ A GLANCE

A comprehensive update on cardiovascular surgery: challenges and opportunities



Filippo Crea [1,2]

[1]Department of Cardiovascular Medicine, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; and [2]Department of Cardiovascular and Pulmonary Sciences, Catholic University of the Sacred Heart, Rome, Italy

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This Focus Issue on cardiac and vascular surgery contains the meta-analysis '**Sex differences in outcomes after coronary artery bypass grafting: a pooled analysis of individual patient data**' by Mario Gaudino from Weill Cornell Medicine in New York, USA, and colleagues.[1] Coronary artery bypass grafting (CABG) is the best therapeutic option in a large subset of patients with severe coronary artery disease.[2–5] The authors note that data suggest that women have worse outcomes than men after CABG, but results have been inconsistent across studies. Due to the large differences in baseline characteristics between sexes, suboptimal risk adjustment due to low-quality data may be the reason for the observed differences. To overcome this limitation, they undertook a systematic review and pooled analysis of high-quality individual patient data from large CABG trials to compare the adjusted outcomes of women and men. The primary outcome was a composite of all-cause mortality, myocardial infarction (MI), stroke, and repeat revascularization [major adverse cardiac and cerebrovascular events (MACCE)]. The secondary outcome was all-cause mortality. Multivariable mixed-effect Cox regression was used. Four trials involving 13 193 patients (10 479 males + 2714 females) were included. Over 5 years of follow-up, women had a significantly higher risk of MACCE [adjusted hazard ratio (HR) 1.12; $P = 0.004$] but similar mortality (adjusted HR 1.03; $P = 0.51$) compared with men. Women had a higher incidence of MI (adjusted HR 1.30; 95% CI 1.11–1.52) and repeat revascularization (adjusted HR 1.22; 95% CI 1.04–1.43), but not stroke (adjusted HR 1.17; 95% CI 0.90–1.52). The difference in MACCE between sexes was not significant in patients 75 years and older. The use of off-pump surgery and multiple arterial grafting did not modify the difference between sexes (*Figure* 1).

Gaudino *et al.* conclude that women have worse outcomes than men in the first 5 years after CABG. This difference is not significant in patients aged over 75 years and is not affected by the surgical technique. The article is accompanied by an **Editorial** by Jolanda Kluin from Amsterdam University Medical Centers and Sanne Peters from Utrecht University in the Netherlands.[6] The authors note that a fundamental issue underpinning the uncertainties in factors underlying sex differences in coronary heart disease (CHD) is the persistent under-representation of women in medical research, including in trials of CHD drugs. Also, even when a sufficient number of women are included, sex-disaggregated analyses are often not conducted and/or discussed adequately. Hence, while studies such as those by Gaudino *et al.* are essential in closing the evidence gap, concerted efforts are needed to dismantle the social, behavioural, pathophysiological, and clinical factors underpinning sex differences in outcomes of CABG and to translate those into medical education, clinical guidelines, and clinical practice. This will lead to new mechanistic insights and improved preventive, diagnostic, and therapeutic targets, and will improve health outcomes for women and men, and reduce health inequalities.

The global burden of peripheral artery disease (PAD) is substantial.[7–9] PAD revascularization can be performed by either an endovascular or open surgical approach. In a Clinical Research article entitled '**Long-term outcomes following endovascular and surgical revascularization for peripheral artery disease: a propensity score-matched analysis**', Saman Parvar from the University of Adelaide in Australia, and colleagues note that despite increasing use of endovascular revascularization, it is still uncertain which strategy yields better long-term outcomes.[10] This retrospective cohort study evaluated patients hospitalized with PAD in Australia and New Zealand who underwent either endovascular or surgical revascularization between 2008 and 2015, and compared procedures using a propensity score-matched analysis. Hybrid interventions were excluded. The primary endpoint was mortality or major adverse limb events (MALE), defined as a composite endpoint of acute limb ischaemia, urgent surgical or endovascular reinterven-

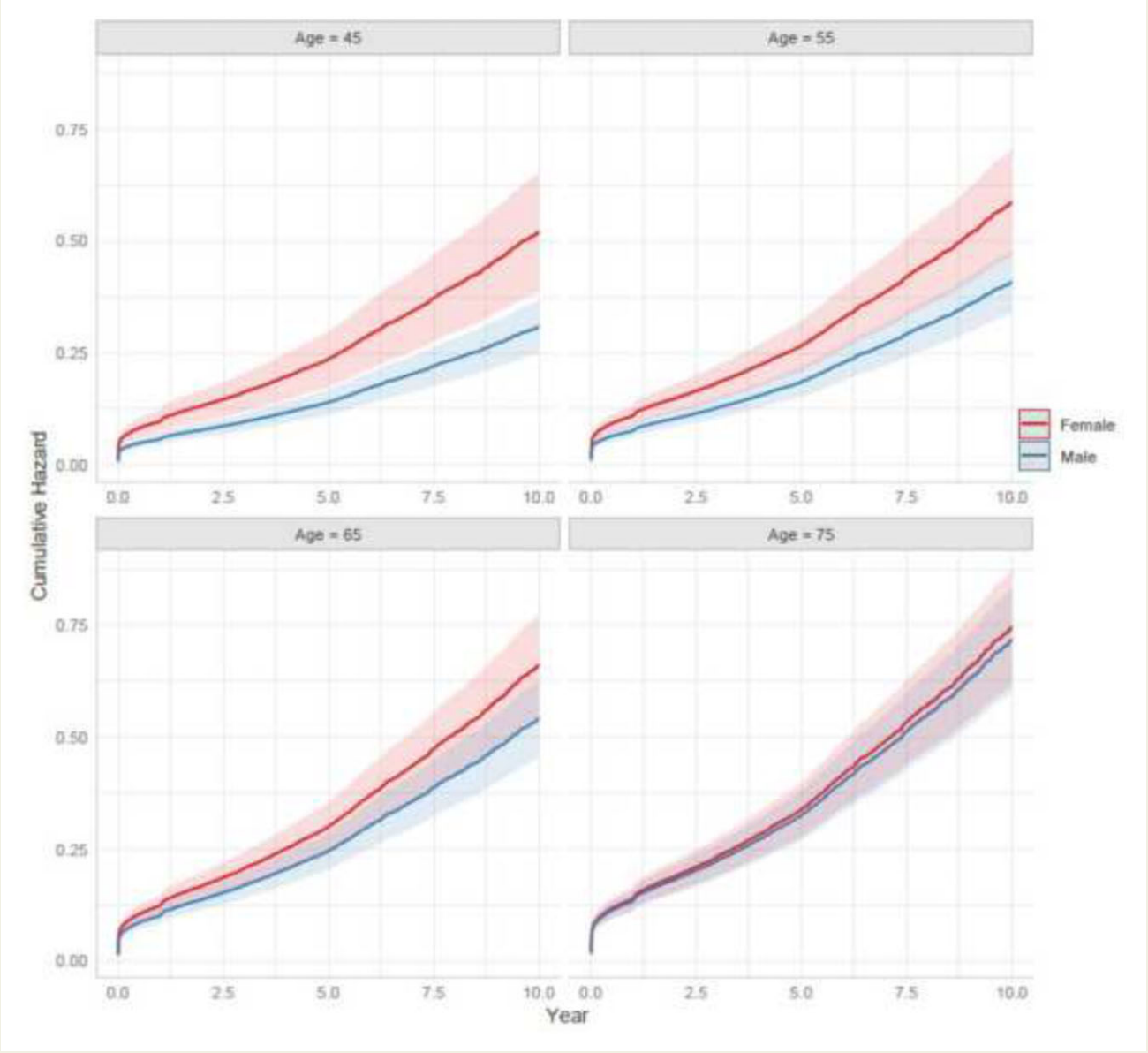

Figure 1 Association of sex across age groups with major adverse cardiac and cerebrovascular events (all-cause mortality/myocardial infarction/stroke/repeat revascularization) from Gaudino M, Di Franco A, Alexander JH, Bakaeen F, Egorova N, Kurlansky P, Boening A, Chikwe J, Demetres M, Devereaux PJ, Diegeler A, Dimagli A, Flather M, Hameed I, Lamy A, Lawton JS, Reents W, Robinson NB, Audisio K, Rahouma M, Serruys PW, Hara H, Taggart DP, Girardi LN, Fremes SE, Benedetto U. Sex differences in outcomes after coronary artery bypass grafting: a pooled analysis of individual patient data. See pages 18–28).

tion, or major amputation, up to 8 years post-hospitalization using time-to-event analyses. A total of 14 339 matched pairs (mean ± SD age 71 ± 12 years, 73% male) with good covariate balance were identified. Endovascular revascularization was associated with an increase in combined MALE or mortality (HR 1.13; $P < 0.001$). There was a similar risk of MALE (HR 1.04; $P = 0.15$) but higher mortality (HR 1.16; $P < 0.001$) when endovascular repair was compared with surgery. In subgroup analysis, these findings were consistent for both claudication and chronic limb-threatening ischaemia presentations.

The authors conclude that although the long-term risk of MALE was comparable for both approaches, enduring advantages of surgical revascularization included lower long-term mortality. This is at odds with some prior PAD studies and highlights contention in this space. The contribution is accompanied by an **Editorial** by Christian-Alexander Behrendt from the University Medical Center Hamburg-Eppendorf in Germany.[11] Behrendt concludes that the study by Parvar and colleagues used a robust design to generate important hypotheses that should be addressed in future studies. Until more comparative effectiveness data from high-quality trials become available, an open-minded multidisciplinary approach and regular case discussions may help to find a way through inconsistent or missing evidence.

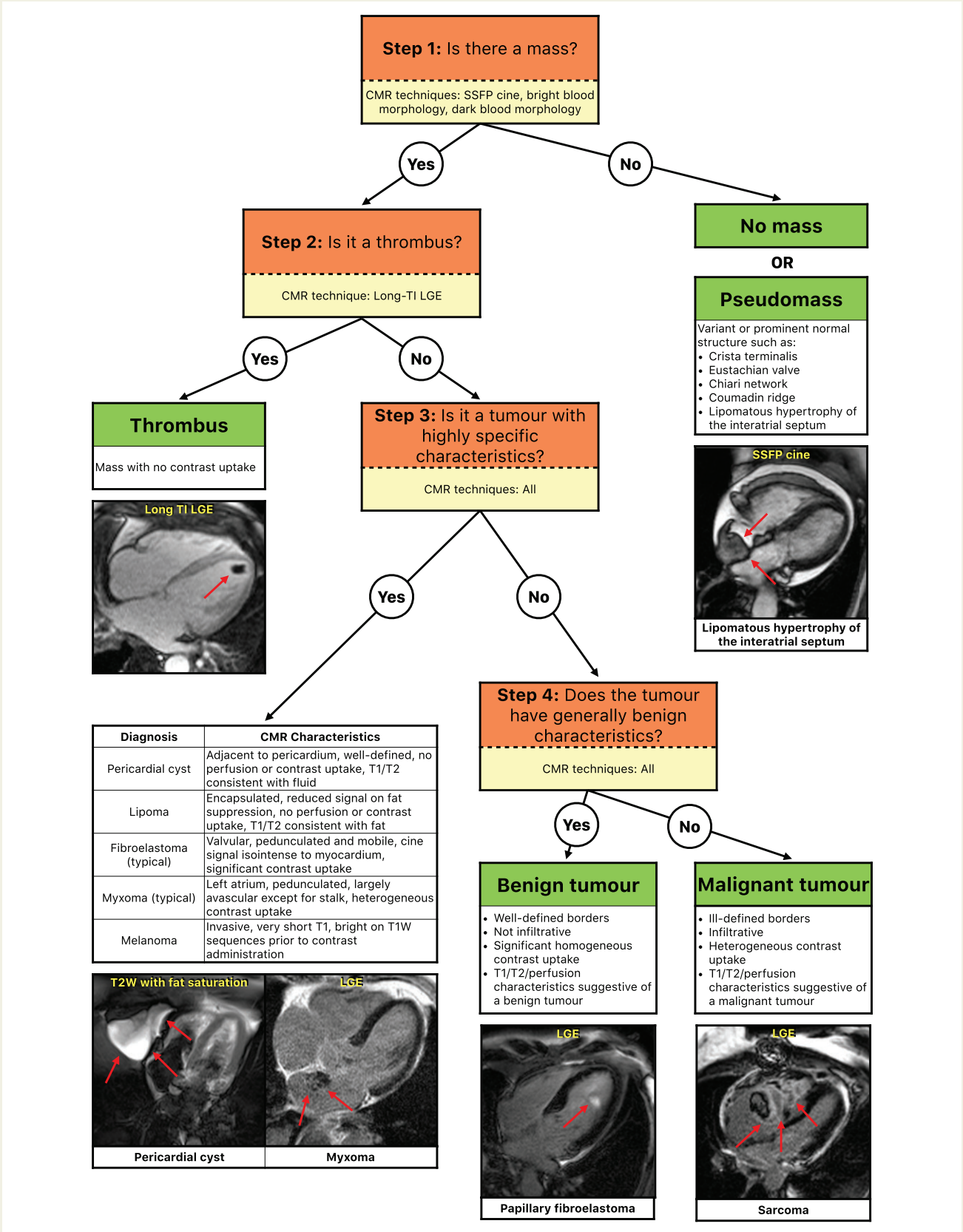

Figure 2 Stepwise algorithm used for cardiovascular magnetic resonance interpretation of patients with suspected cardiac tumour. CMR, cardiovascular magnetic resonance; LGE, late gadolinium enhancement; SSFP, steady-state free precession (from Shenoy C, Grizzard JD, Shah DJ, Kassi M, Reardon MJ, Zagurovskaya M, Kim HW, Parker MA, Kim RJ. Cardiovascular magnetic resonance imaging in suspected cardiac tumour: a multicentre outcomes study. See pages 71–80).

Acute aortic dissection (AAD) is frequently a challenging surgical emergency.[12–14] Operability of type A AAD (TAAAD) is currently based on a non-standardized decision-making process, and it lacks a disease-specific risk evaluation model that can predict mortality. In a Clinical Research article entitled '**Determinants of outcomes following surgery for type A acute aortic dissection: the UK National Adult Cardiac Surgical Audit**', Umberto Benedetto from the University of Bristol in the UK, and colleagues investigated patient, intra-operative data, surgeon, and centre-related variables for patients who underwent TAAAD in the UK.[15] The authors identified 4203 patients undergoing TAAAD surgery in the UK (2009–2018), who were enrolled into the UK National Adult Cardiac Surgical Audit dataset. The primary outcome was operative mortality. Variations related to hospital or surgeon effects were quantified by a generalized mixed linear model and risk-adjusted funnel plots by displaying the individual standardized mortality ratio against expected deaths. Independent predictive variables of mortality were: age [odds ratio (OR) 1.02; $P < 0.001$]; malperfusion (OR 1.79; $P < 0.001$); left ventricular ejection fraction (moderate: OR 1.40; $P = 0.001$; poor: OR 2.83; $P < 0.001$); previous cardiac surgery (OR 2.29; $P < 0.001$); pre-operative mechanical ventilation (OR 2.76; $P < 0.001$); pre-operative resuscitation (OR 3.36; $P = 0.028$); and concomitant CABG (OR 2.29; $P < 0.001$). The authors found a significant inverse relationship between surgeons but not centre annual volume with outcomes.

Benedetto and colleagues conclude that patient characteristics, intra-operative factors, and high-volume surgeons are strong determinants of outcomes following TAAAD surgery. These findings may help in refining clinical decision-making, supporting patient counselling, and be used by policy makers for quality assurance and service provision improvement. This paper is accompanied by an **Editorial** by Martin Czerny and Bartosz Rylski from the University Heart Center Freiburg in Bad Krozingen, Germany.[16] The authors highlight that—in summary—its all about the location of the primary entry tear as well as the presence or absence of malperfusion. This knowledge, together with the routine application of the TEM classification and the GERAADA score, mirrors the development of AAD to the archetype of personalized aortic medicine and will help in further refinement of therapeutical strategies, leading to better outcome in the years to come.

The choice between percutaneous coronary interventions (PCIs) and CABG remains controversial.[5,17] In a Clinical Research article entitled '**Ten-year all-cause death after percutaneous or surgical revascularization in diabetic patients with complex coronary artery disease**', Rutao Wang from the National University of Ireland, and colleagues sought to compare rates of all-cause death at 10 years following CABG or PCI in patients with or without diabetes.[18] The SYNTAXES study evaluated up to 10-year survival of 1800 patients with three-vessel disease (3VD) and/or left main coronary artery disease (LMCAD) randomized to receive either PCI or CABG in the SYNTAX trial. In diabetics, the risk of mortality was numerically higher with PCI compared with CABG at 5 years (19.6% vs. 13.3%, HR 1.53; $P = 0.075$), with the opposite seen between 5 and 10 years (PCI vs. CABG 20.8% vs. 24.4%, HR 0.82; $P = 0.366$). Irrespective of diabetic status, there was no significant difference in all-cause death at 10 years between patients receiving PCI or CABG; the absolute treatment difference was 1.9% in diabetics (PCI vs. CABG 36.4% vs. 34.5%, difference 1.9%; $P = 0.551$). Among insulin-treated patients, all-cause death at 10 years was numerically higher with PCI (47.9% vs. 39.6%, difference 8.2%; $P = 0.227$).

Wang *et al.* conclude that the treatment effects of PCI vs. CABG on all-cause death at 10 years in patients with 3VD and/or LMCAD were similar irrespective of the presence of diabetes. There may, however, be a survival benefit with CABG in patients with insulin-treated diabetes. The association between revascularization strategy and very long-term ischaemic and safety outcomes for patients with diabetes needs further investigation in dedicated trials. This manuscript is accompanied by an **Editorial** by William E. Boden from the Boston University School of Medicine, Raffaele De Caterina from the University of Pisa, and David Taggart from Oxford University.[19] The authors conclude that the methodology used by Wang *et al.* in this SYNTAX analysis raises several major concerns that seriously challenge their conclusions that 10-year all-cause mortality was not different in diabetic patients treated with either PCI or CABG, and that diabetes did not discriminate any between-group differences in mortality.

Finally, in a Clinical Research article entitled '**Cardiovascular magnetic resonance imaging in suspected cardiac tumour: a multicentre outcomes study**', Chetan Shenoy from the University of Minnesota and colleagues note that cardiovascular magnetic resonance (CMR) imaging is a key diagnostic tool for the evaluation of patients with suspected cardiac tumours.[20] In this multicentre study of patients undergoing clinical CMR for suspected cardiac tumour, CMR diagnoses were assigned as no mass, pseudomass, thrombus, benign tumour, or malignant tumour. A final diagnosis was determined after follow-up using all available data. The primary endpoint was all-cause mortality. Among 903 patients, the CMR diagnosis was no mass in 25%, pseudomass in 16%, thrombus in 16%, benign tumour in 17%, and malignant tumour in 23%. Over a median of 4.9 years, 376 patients died. Compared with the final diagnosis, the CMR diagnosis was accurate in 98.3% of patients. Patients with CMR diagnoses of pseudomass and benign tumour had similar mortality to those with no mass, whereas those with malignant tumour (HR 3.31) and thrombus (HR 1.46) had significantly greater mortality. The CMR diagnosis provided incremental prognostic value over clinical factors including left ventricular ejection fraction, coronary artery disease, and history of extracardiac malignancy ($P < 0.001$) (*Figure* 2).

The authors conclude that in patients with suspected cardiac tumour, CMR has high diagnostic accuracy. Patients with CMR diagnoses of no mass, pseudomass, and benign tumour have similar long-term mortality. The CMR diagnosis is a powerful independent predictor of mortality incremental to clinical risk factors. This manuscript is accompanied by an **Editorial** by Grigorios Korosoglou from GRN Hospital Weinheim, Germany and colleagues.[21] The authors conclude that the study by Shenoy *et al.* represents a very important step towards establishing the role of CMR not only for the diagnostic classification but also for the precise risk stratification of patients with suspected cardiac tumours. Further multicentre studies are now warranted, investigating the specific use of multimodal imaging, including echocardiography, CMR, cardiac computed tomography, and positron emission tomography for the diagnostic work-up and the risk stratification of such patients.

The issue is also complemented by two Discussion Forum contributions. In a commentary entitled '**Right ventricle assessment in patients with pulmonary embolism: low risk = low yield for systematic echocardiography**', Lars C Huber and Mattia Arrigo from the University of Zurich in Switzerland comment on the recent publication '**Right ventricle assessment in patients with pulmonary embolism at low risk for death based on clinical models: an individual patient data meta-analysis**' by Cecilia Becattini from the University of Perugia in Italy, and colleagues.[22,23] Becattini *et al*. respond in a separate comment.[24]

The editors hope that this issue of the *European Heart Journal* will be of interest of its readers.

References

1. Gaudino M, Di Franco A, Alexander JH, Bakaeen F, Egorova N, Kurlansky P, Boening A, Chikwe J, Demetres M, Devereaux PJ, Diegeler A, Dimagli A, Flather M, Hameed I, Lamy A, Lawton JS, Reents W, Robinson NB, Audisio K, Rahouma M, Serruys PW, Hara H, Taggart DP, Girardi LN, Fremes SE, Benedetto U. Sex differences in outcomes after coronary artery bypass grafting: a pooled analysis of individual patient data. *Eur Heart J* 2022;**43**:18–28.
2. Völz S, Redfors B, Angerås O, Ioanes D, Odenstedt J, Koul S, Valeljung I, Dworeck C, Hofmann R, Hansson E, Venetsanos D, Ulvenstam A, Jernberg T, Råmunddal T, Pétursson P, Fröbert O, Erlinge D, Jeppsson A, Omerovic E. Long-term mortality in patients with ischaemic heart failure revascularized with coronary artery bypass grafting or percutaneous coronary intervention: insights from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR). *Eur Heart J* 2021;**42**:2657–2664.
3. Schoenrath F, Just IA, Falk V, Emmert MY. Antiplatelet and direct oral anticoagulation management after coronary artery bypass graft surgery: the Cinderella of current cardiovascular trials, please show me (some) evidence. *Eur Heart J* 2021; **42**:2145–2148.
4. Ben-Yehuda O, Chen S, Redfors B, McAndrew T, Crowley A, Kosmidou I, Kandzari DE, Puskas JD, Morice MC, Taggart DP, Leon MB, Lembo NJ, Brown WM, Simonton CA, Dressler O, Kappetein AP, Sabik JF, Serruys PW, Stone GW. Impact of large periprocedural myocardial infarction on mortality after percutaneous coronary intervention and coronary artery bypass grafting for left main disease: an analysis from the EXCEL trial. *Eur Heart J* 2019;**40**:1930–1941.
5. Davierwala PM, Gao C, Thuijs DJFM, Wang R, Hara H, Ono M, Noack T, Garg S, O'Leary N, Milojevic M, Kappetein AP, Morice MC, Mack MJ, van Geuns RJ, Holmes DR Jr, Gaudino M, Taggart DP, Onuma Y, Mohr FW, Serruys PW; for the SYNTAX Extended Survival Investigators. Single or multiple arterial bypass graft surgery vs. percutaneous coronary intervention in patients with three-vessel or left main coronary artery disease. *Eur Heart J* 2021;doi:10.1093/eurheartj/ehab537.
6. Peters SAE, Kluin J. Why do women do worse after coronary artery bypass grafting? *Eur Heart J* 2022;**43**:29–31.
7. Aboyans V, Bauersachs R, Mazzolai L, Brodmann M, Palomares JFR, Debus S, Collet JP, Drexel H, Espinola-Klein C, Lewis BS, Roffi M, Sibbing D, Sillesen H, Stabile E, Schlager O, De Carlo M. Antithrombotic therapies in aortic and peripheral arterial diseases in 2021: a consensus document from the ESC working group on aorta and peripheral vascular diseases, the ESC working group on thrombosis, and the ESC working group on cardiovascular pharmacotherapy. *Eur Heart J* 2021;**42**:4013–4024.
8. Wadström BN, Wulff AB, Pedersen KM, Jensen GB, Nordestgaard BG. Elevated remnant cholesterol increases the risk of peripheral artery disease, myocardial infarction, and ischaemic stroke: a cohort-based study. *Eur Heart J* 2021;doi: 10.1093/eurheartj/ehab705.
9. Krantz MJ, Debus SE, Hsia J, Patel MR, Anand SS, Nehler MR, Hess CN, Capell WH, Bracken T, Szarek M, Mátyás L, Krievins DK, Nault P, Stefanov S, Haskell LP, Berkowitz SD, Muehlhofer E, Hiatt WR, Bauersachs RM, Bonaca MP. Low-dose rivaroxaban plus aspirin in older patients with peripheral artery disease undergoing acute limb revascularization: insights from the VOYAGER PAD trial. *Eur Heart J* 2021;**42**:4040–4048.
10. Parvar SL, Ngo L, Dawson J, Nicholls SJ, Fitridge R, Psaltis PJ, Ranasinghe I. Long-term outcomes following endovascular and surgical revascularization for peripheral artery disease: a propensity score-matched analysis. *Eur Heart J* 2022;**43**: 32–40.
11. Behrendt CA. Higher long-term mortality after endovascular vs. open-surgical revascularization of peripheral artery disease in Australia and New Zealand? *Eur Heart J* 2022;**43**:41–43.
12. Chen J, Gao Y, Jiang Y, Li H, Lv M, Duan W, Lai H, Chen R, Wang C. Low ambient temperature and temperature drop between neighbouring days and acute aortic dissection: a case–crossover study. *Eur Heart J* 2021;doi:10.1093/eurheartj/ehab803.
13. Al-Hussaini A. Pregnancy and aortic dissections. *Eur Heart J* 2020;**41**: 4243–4244.
14. Beyer SE, Dicks AB, Shainker SA, Feinberg L, Schermerhorn ML, Secemsky EA, Carroll BJ. Pregnancy-associated arterial dissections: a nationwide cohort study. *Eur Heart J* 2020;**41**:4234–4242.
15. Benedetto U, Dimagli A, Kaura A, Sinha S, Mariscalco G, Krasopoulos G, Moorjani N, Field M, Uday T, Kendal S, Cooper G, Uppal R, Bilal H, Mascaro J, Goodwin A, Angelini G, Tsang G, Akowuah E; on the behalf of UK Aortic group. Determinants of outcomes following surgery for type A acute aortic dissection: the UK National Adult Cardiac Surgical Audit. *Eur Heart J* 2022;**43**:44–52.
16. Czerny M, Rylski B. Acute type A aortic dissection reconsidered: it's all about the location of the primary entry tear and the presence or absence of malperfusion. *Eur Heart J* 2022;**43**:53–55.
17. Windecker S, Neumann FJ, Jüni P, Sousa-Uva M, Falk V. Considerations for the choice between coronary artery bypass grafting and percutaneous coronary intervention as revascularization strategies in major categories of patients with stable multivessel coronary artery disease: an accompanying article of the task force of the 2018 ESC/EACTS guidelines on myocardial revascularization. *Eur Heart J* 2019;**40**:204–212.
18. Wang R, Serruys PW, Gao C, Hara H, Takahashi K, Ono M, Kawashima H, O'Leary N, Holmes DR, Witkowski A, Curzen N, Burzotta F, James S, van Geuns RJ, Kappetein AP, Morel MA, Head SJ, Thuijs DJFM, Davierwala PM, O'Brien T, Fuster V, Garg S, Onuma Y. Ten-year all-cause death after percutaneous or surgical revascularization in diabetic patients with complex coronary artery disease. *Eur Heart J* 2022;**43**:56–67.
19. Boden WE, De Caterina R, Taggart DP. Is there equivalence between PCI and CABG surgery in long-term survival of patients with diabetes? Importance of interpretation biases and biological plausibility. *Eur Heart J* 2022;**43**:68–70.
20. Shenoy C, Grizzard JD, Shah DJ, Kassi M, Reardon MJ, Zagurovskaya M, Kim HW, Parker MA, Kim RJ. Cardiovascular magnetic resonance imaging in suspected cardiac tumour: a multicentre outcomes study. *Eur Heart J* 2022;**43**: 71–80.
21. Giusca S, Kelle S, Korosoglou G. When tissue and outcomes are the issue. Cardiac magnetic resonance for patients with suspected cardiac tumours. *Eur Heart J* 2022;**43**:81–83.
22. Arrigo M, Huber LC. Right ventricle assessment in patients with pulmonary embolism: low risk = low yield for systematic echocardiography. *Eur Heart J* 2022; **43**:84–85.
23. Becattini C, Maraziti G, Vinson DR, Ng ACC, den Exter PL, Côté B, Vanni S, Doukky R, Khemasuwan D, Weekes AJ, Soares TH, Ozsu S, Polo Friz H, Erol S, Agnelli G, Jiménez D. Right ventricle assessment in patients with pulmonary embolism at low risk for death based on clinical models: an individual patient data meta-analysis. *Eur Heart J* 2021;**42**:3190–3199.
24. Maraziti G, Vinson DR, Becattini C. Echocardiography for risk stratification in patients with pulmonary embolism at low risk of death: a response. *Eur Heart J* 2022;**43**:86–87.