msj Medicine & Science Journal

Medicine & Science Journal 2023; 1(1):e202336
https://doi.org/10.53150/msj.v1i1.36

REVIEW ARTICLE

2022 highlights in interventional cardiology

Novel concepts for multivessel coronary artery disease treatment, vascular access for coronary interventions, and heart valve interventions

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In 2022 much new evidence-based information related to coronary and structural interventions has been published, and several trials offered new therapies and practice-changing insights for patients with advanced ischemic and structural heart disease. Therefore, this review highlights some of the most exciting data from the latest published manuscripts in the interventional cardiology field. In our report, we tried to address the strengths and weaknesses of every piece of evidence, searching for a balance between nonconstructive criticism and easy enthusiasm.

Coronary artery disease treatment in patients with left ventricular dysfunction

Coronary artery disease is the most common cause of heart failure and is associated with poor survival and low quality of life despite advances in medical therapy[1]. In the ESC guidelines, coronary artery bypass graft (CABG) is recommended as the first revascularization strategy in patients with ischemic cardiomyopathy and multivessel disease as long as the risk of surgery is acceptable (class I, level of evidence B)[2,3]. Percutaneous Coronary Intervention (PCI) can be considered in one- or two-vessel disease when complete revascularisation can be achieved (or in three-vessel disease based on advice from the heart team). However, that recommendation is relatively weak (class IIa, level of evidence C). CABG is also recommended in the USA for the same clinical context, and no clear indication

Received: April 3, 2023
Revised: July 10, 2023
Accepted: September 20, 2023
Published: September 27, 2023

Article information are listed at the end of this article.

for PCI has been established due to limited evidence[4]. In 2022 the REVIVED-BCIS2 randomized controlled trial tried to shed light on this controversial topic. The study, whose protocol and results were published in the Journal of the American College of Cardiology[5] and the New England Medical Journal[6], claimed that PCI did not reduce all-cause mortality or hospitalizations for heart failure in patients with severe left ventricular dysfunction and extensive coronary artery disease. Restoring the patency of coronary arteries to improve blood supply to jeopardized, stunned or hibernating myocardium has long been considered a must-to-have treatment in this highest-risk patient population. In the STICH trial, coronary revascularization was accomplished through CABG, but treatment improved survival only in highly selected, typically young, patients. Moreover, the benefit needed a ten-year follow-up to emerge, probably due to the required time for CABG benefits to counterbalance the early surgical complications. PCI is from ever perceived as an attractive alternative to bypass surgery, as it might offer the benefits of revascularisation without the early surgical hazards[7, 8]. However, when dealing with patients with left ventricular dysfunction and obstructive coronary disease, no randomized evidence supports percutaneous revascularization, and according to expert opinion and local practice and expertise, this treatment is recommended only in selected patients.

The REVIVED-BCIS2 is the first adequately powered randomized trial to examine the efficacy and safety of PCI in patients with left ventricular systolic dysfunction and angiographically significant coronary artery disease[6]. The study enrolled patients with severe left ventricular dysfunction (ejection fraction 35% or below), extensive coronary artery disease, and demonstrable viability in at least four dysfunctional myocardial segments potentially addressable by percutaneous revascularization. Any commonly accepted diagnostic modality could assess viability, but cardiac magnetic resonance imaging was used the most. Recent myocardial infarction within four weeks, decompensated heart failure, or sustained ventricular arrhythmias within 72 hours were criteria for exclusion from the study. A total of 700 patients from 40 centres in the UK were randomly assigned in a 1:1 ratio to either PCI with optimal medical therapy or optimal medical therapy alone. The median age of participants was 70 years, 88% were men, and their mean left ventricular ejection fraction was 28%. The primary outcome was the composite endpoint of all-cause death or hospitalization for heart failure. Secondary outcomes included left ventricular ejection fraction at six and 12 months and quality of life measures. During a median follow-up of 3.4 years, the primary outcome occurred in 129 (37.2%) patients in the PCI group and 134 (38.0%) patients in the medical therapy alone group with a hazard ratio of 0.99 (95% confidence interval 0.78–1.27, p=0.96). No significant difference between groups was observed for the trial's most clinically significant secondary outcome, the left ventricular ejection fraction at six and 12 months.

Given that only patients with demonstrable myocardial viability were enrolled, the latter finding challenges the concept of myocardial hibernation. This phenomenon, first described by Rahimtoola in 1989[9], for decades has been considered an adaptation of the heart to cope with the effects of severe coronary disease, potentially reversible by restoring coronary patency[10]. Quality of life (the other most significant secondary outcome) favoured PCI at 6 and 12 months, but differences between groups were no more demonstrable at 24 months. However, it is essential to note that REVIVED-BCIS2 excluded patients with limiting angina or recent acute coronary syndromes, and PCI is still an option in these contexts.

CABG vs. PCI in patients with multivessel coronary artery disease

CABG and PCI for patients with multivessel coronary disease have been compared in many studies with non-univocal results[10-13]. Recently, the long-term follow-up of the BEST trial, which compared multivessel PCI performed with everolimus-eluting stents vs. CABG in patients with multivessel coronary artery disease, has been published[14]. The study was prematurely terminated in 2013, as at that time, only 880 of the planned 1776 patients had been enrolled[15]. In the BEST trial last report, PCI and CABG groups showed no significant long-term difference in all-cause death, MI, or target-vessel revascularisation. These observations were in line with the earlier reports of the study[15]. However, after 11.8 years of follow-up, PCI, compared with CABG, was associated with an excess of spontaneous MI (7.1% vs. 3.8%) and repeated revascularisations (22.6% vs. 12.7%). Long-term mortality was similar between treatment groups (20.5% vs. 19.9%). Interestingly, the excess of strokes reported in patients treated with CABG in most previous studies was not apparent in the BEST trial.

 https://doi.org/10.53150/msj.v1i1.36

Finally, this study was conducted in South Korea, and its findings may not apply to Western Countries patients.

Physiology-guided CABG for patients with multivessel coronary artery disease

From the coronary functional point of view, we want to remember that a substudy from the FAME 3 trial assessed the impact of post-PCI fractional flow reserve (FFR) and intravascular imaging on patient and lesion outcomes[16]. As known, the results of FAME 3 indicated that FFR-guided PCI using current-generation drug-eluting stents did not meet the criteria for non-inferiority compared with CABG among patients with angiographic three-vessel disease[17]. In this new analysis, only 61% had FFR measured following PCI, which was not required by the study protocol (43% one-vessel, 42% two-vessel, 15% three-vessel). In patients evaluated with FFR after PCI, the median final FFR measurement was 0.89; in 10% of patients, FFR was ≤0.80, despite angiographically successful intervention. Furthermore, an abnormal FFR after PCI significantly predicted target vessel failure using a cut-off value of 0.88 at the vessel level and 0.85 at the patient level. Moreover, only 11.1% of patients had intravascular imaging following PCI. In the study, the rate of cardiac death, MI, and repeat revascularisation was similar among the patients who did and did not have intravascular imaging guidance.

Ultrasound-guided access for transfemoral coronary interventions

The need for ultrasound guidance for vascular access is a hot topic, made even more actual with the current decrease in femoral vascular access in favour of the transradial route for routine and urgent coronary interventions. However, attention has returned to femoral artery access because the rate of structural heart interventions is steeply increasing. UNIVERSAL, a multicentre randomized clinical trial that compared ultrasonography-guided femoral access vs. fluoroscopy-guided femoral access in patients undergoing coronary angiography or PCI via femoral access, showed no benefit in using ultrasonography as a guide[18]. However, the randomized population was not consecutive patients undergoing diagnostic angiography, as many cases at these centres were performed with transradial access. Instead, they were selected patients chosen for transfemoral access due to anatomic considerations related to the radial artery or operator preference. Access sheath sizes were nearly all 6F or 7F, and approximately half of the cases were performed by fellows in training, as the trial was conducted at academic medical institutions. The investigators found that ultrasonography-guided access did not significantly reduce the risk of their primary outcome (a composite of Bleeding Academic Research Consortium grade 2, 3, or 5, bleeding at 30 days, and major periprocedural vascular complications). However, ultrasonography-guided access did reduce the time to obtain access, the need for multiple attempts at arterial puncture, and the incidence of inadvertent venipuncture. In a prespecified, nonrandomized subset of patients treated with a vascular closure device placed via operator discretion, a group with a considerably higher rate of vascular complications and bleeding, ultrasonography-guidance was associated with a reduction in risk of the primary outcome (11.8% vs. 23.4%; odds ratio, 0.44; 95% CI, 0.23-0.82). It is worth noting that the ultrasonography group in UNIVERSAL had a higher first-pass success rate and that, as stated before, very few patients with large-bore access were included in this study. A more significant benefit might have been observed in this setting with routine ultrasonography guidance. Until more evidence emerges or a meta-analysis is published that combines the data from the UNIVERSAL trial with data from other trials, it seems reasonable to use ultrasound-guided access for the femoral artery for coronary angiography and intervention and for large-bore vascular access for mechanical circulatory support and structural heart intervention.

Novel evidence in transcatheter valvular interventions

Turning to degenerative mitral valve disease, a novel transcatheter edge-to-edge repair (TEER) system called PASCAL was evaluated in the CLASP IID trial[19]. The CLASP IID randomized trial is the first to evaluate the safety and effectiveness of the PASCAL system compared with the MitraClip system in patients with significant symptomatic degenerative mitral regurgitation (DMR). The researchers randomized 180 patients (mean age 81 years, 33% women) with DMR at high surgical risk (3+ or 4+ mitral regurgitation grade) to the PASCAL or MitraClip system. The trial demonstrated that the PASCAL system was non-inferior to the MitraClip system for the primary

 https://doi.org/10.53150/msj.v1i1.36

safety endpoint of major adverse events (cardiovascular mortality, stroke, myocardial infarction, new need for renal replacement therapy, severe bleeding, non-elective mitral valve reintervention for 30 days), occurring in 3.4% and 4.8% of the patient groups, respectively ($p<0.05$). Cardiovascular mortality occurred in 0.9% and 1.6% of the respective groups. Although CLASP IID was a non-inferiority trial, it will expand treatment options for patients with severe degenerative valve disease. Ongoing studies compare TEER with MitraClip versus surgical mitral valve repair in patients with degenerative MR. One of those studies, PRIMARY, is a superiority trial funded by the National Institutes of Health with a planned enrolment of 450 patients at all levels of surgical risk. The other study is REPAIR MR, a non-inferiority study testing MitraClip versus valve repair surgery in intermediate-risk DMR patients. At last, the CLASP IIF study is also ongoing. In that study, investigators compare PASCAL to MitraClip in patients with functional mitral regurgitation and high surgical risk.

Finally, moving to aortic valve disease, the PROTECTED TAVR trial with 3000 patients found that the routine use of intraprocedural cerebral embolic protection (CEP) did not reduce the primary outcome of risk of stroke within 72 hours among patients undergoing transfemoral TAVR for aortic stenosis (2.3% vs. 2.9% with control)[20]. However, although this was a negative trial, there was a significant reduction in the secondary outcome of disabling strokes in the CEP vs. control group (0.5% vs. 1.3%; $p<0.05$).

Table 1. P2022 most relevant studies in Interventional Cardiology

Study Name	Description	Population	Primary Endpoint	Result
REVIVED-BCIS2	PCI vs. OMT in patients with EF<35% and extensive CAD	700 pts 1:1 allocation	All-cause death or hospitalization for heart failure	No differences
BEST	Multivessel PCI performed with everolimus-eluting stents vs. CABG	880 pts 1:1 allocation	All-cause death, MI, or target-vessel revascularisation at 11.8 yrs	No differences
FAME 3 substudy	FFR and imaging after PCI in predicting TLF	757 pts from the PCI arm of the FAME 3 trial. 61% had FFR, 11.1% had imaging	TLF	FFR predicts TLF with the cutoff of 0.88. Imaging use did not affect TLF
UNIVERSAL	Ultrasonography-guided femoral access vs. fluoroscopy-guided femoral access in patients undergoing coronary angiography or PCI	621 pts 1:1 allocation	BARC grade 2, 3, or 5, bleeding at 30 days, and major periprocedural vascular complications	No differences
CLASP II	PASCAL vs. MitraClip in patients with significant symptomatic degenerative mitral regurgitation	180 pts 1:1 allocation	Cardiovascular mortality, stroke, myocardial infarction, new need for renal replacement therapy, severe bleeding, non-elective mitral valve reintervention for 30 days	Non inferiority
PROTECTED TAVR	Routine use of intraprocedural CEP in patients undergoing transfemoral TAVR for aortic stenosis	3000 pts 1:1 allocation	Stroke at 72 h	No differences

https://doi.org/10.53150/msj.v1i1.36

Conclusions

In a nutshell, we can summarize some very important take home messages from the 2022 studies. First of all, treating coronary artery disease with PCI in patients with left ventricular dysfunction may not not reduce MACE, but only in patients with in very stable clinical setting, since we have no data in patients affected by limiting angina and recent ACS.

Secondly, CABG vs. PCI in patients with multivessel coronary artery disease is an ongoing debate, with new evidence that confirms what we should expect from clinical practice: more short-term adverse events in CABG and more long term adverse events in PCI. This means that we probably should consider at most patient age than other clinical variables in our decision-making process.

Moving to physiology, FFR measurement after PCI predicts target vessel failure with a cutoff that is different from the one commonly used to define a de novo critical stenosis. Interventionalist should be aware of this in order to change their view in their PCIs.

Talking about ultrasound-guided access for transfemoral interventions, use ultrasound-guided access for the femoral artery has confirmed its safety, especially in interventions that require large-bore vascular access, even if data about adverse clinical events are not significantly lower with this approach.

Finally, transcatheter edge-to-edge repair for degenerative mitral valve disease could be performed with the new PASCAL device as well as with the well-known Mitraclip, since its non-inferiority has been demonstrated. At last, CEP in TAVR did not demonstrate any superiority in reducing the primary endpoint, but we should keep in mind that a reduction in disabling strokes emerged with the use of CEP.

Indeed 2022 was a very prolific year in terms of new evidence in Interventional Cardiology, but, as always, we must stay hungry and be careful in turning these new data into our clinical practice.

Declarations of interest: none.

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