JORGE THIERER[MTSAC]

Two studies on MINOCA

Mileva N, Paolisso P, Gallinoro E, Fabbricatore D, Munhoz D, Bergamaschi L et al. Diagnostic and Prognostic Role of Cardiac Magnetic Resonance in MINOCA: Systematic Review and Meta-Analysis. **JACC Cardiovasc Imaging 2023;16:376-89. https://doi.org/10.1016/j.jcmg.2022.12.029**

Zeng M, Zhao C, Bao X, Liu M, He L, Xu Y et al. Clinical Characteristics and Prognosis of MINOCA Caused by Atherosclerotic and Nonatherosclerotic Mechanisms Assessed by OCT. **JACC Cardiovasc Imaging 2023;16:521-32. https://doi.org/10.1016/j.jcmg.2022.10.023**.

According to the Fourth Universal Definition of Acute Myocardial Infarction (AMI), the term MINOCA designates an AMI (rising and falling troponins with at least one value above the 99th percentile, plus at least one of the following criteria: symptoms or ECG changes suggestive of ischemia, development of pathologic Q waves, evidence on imaging study, or thrombosis demonstrated on angiography or pathology) in the absence of obstructive coronary disease (≥50 % lesion in any epicardial vessel) and other conditions that might justify the condition (sepsis, aortic dissection, pulmonary embolism, myocarditis, Takotsubo, etc.). The mechanisms responsible may involve the epicardial vessels (spasm, thrombosis in situ, embolism, dissection) or the microcirculation (spasm or microvascular dysfunction). Although the prognosis is better than that of AMI with epicardial coronary disease, it is far from benign, and the recurrence of symptoms is high.

The diagnosis of MINOCA has been defined as a "working diagnosis", since, as can be seen from the definition, after demonstrating the absence of obstructive coronary artery disease on coronary angiography, progress must be made in ruling out alternative causes of the clinical picture. At the time of the suggested diagnostic studies, the Argentine Consensus of MINOCA (Rev Argent Cardiol 2022;90: supl. 2) proposes the assessment of wall motion, invasively with angiographic ventriculography or non-invasively with a Doppler echocardiogram (both studies with IB indication), which help to approximate the diagnosis by defining whether there is a regional alteration (more in favor of a diagnosis of MINOCA) or global, if there is the presence of dissection, cardioembolism (if in doubt, transesophageal echocardiography can be used), etc. In the diagnostic algorithm, cardiac magnetic resonance (CMR) appears next, also with IB indication, for all cases in which diagnostic doubts arise. Demonstration of an ischemic patent on CMR will confirm the diagnosis of MINOCA. Although it is increasingly used, CMR has different strength of indication in different guidelines, and its place in the order of studies varies according to the availability of the resource, costs, etc.

We have just learned about a systematic review and meta-analysis of published studies on the diagnostic and prognostic yield of CMR in the context of the MINOCA presumptive case study. Studies that reported the results of a CMR performed within 10 days of the index event in patients with a "working diagnosis" of MINOCA, and in which the prevalence, beyond confirmation of the presumptive diagnosis, was included of alternative diagnoses: AMI, myocarditis, Takotsubo, or a normal result. A total of 26 studies were included, with 3624 patients, 56% men, with a mean age 54 years. 11% had diabetes, 31% arterial hypertension, 32% dyslipidemia, and 24% were smokers. CMR was performed at a median of 6 days (interquartile range, IQR, 2-9 days). The definitive diagnosis was Takotsubo in 10% of the cases (95% CI 6-12%), myocarditis in 31% (95% CI 25-39%); there were other alternative diagnoses (dilated, hypertrophic, or arrhythmogenic cardiomyopathy) in 10%, and the findings were normal in 27% of cases (95% CI 18-38 %). And the MINOCA? A patent suggestive of AMI was seen in 22% of the studies (95% CI 17-26%), that is, the MINOCA condition was confirmed in one out of every 5 cases. Something that deserves to be highlighted is the high degree of heterogeneity between the different studies in the prevalence of each of the diagnoses mentioned, which for Takotsubo, myocarditis and MINOCA was around 90%. In 5 studies (770 patients, median follow-up 45 months) it was possible to define the prognostic value of CMR findings: while the diagnosis of myocarditis or Takotsubo did not imply a far worse prognosis (OR of 1.09 and 1.16 respectively, in both cases with p=NS), that of MINOCA was associated with a higher risk of major adverse cardiovascular events (OR 2.40, 95% CI 1.60-3.69).

Based on the findings of their meta-analysis, the authors propose a diagnostic algorithm, in which, in patients with a presumptive diagnosis of MINOCA (coronary angiography or coronary CT angiography without evidence of obstructive disease), after having ruled out extracardiac causes of increased troponin (dissection, sepsis, pulmonary embolism, etc.), the immediate step is to perform CMR. The demonstration of an ischemic patent (by compatible findings of late gadolinium enhancement, *T1/T2 mapping* and alteration of the extracellular volume) certifies the diagnosis, and enables, if necessary, to carry out invasive studies that clarify the causal mechanism: intracoronary ultrasound, intracoronary vasoreactivity test, optical coherence tomography (OCT), etc. A non-ischemic patent suggests Takotsubo, myocarditis, other cardiomyopathies. A normal patent (more than a quarter of the cases in the

meta-analysis) leaves the condition without a clear diagnosis.

As we said, the pathophysiology underlying MINOCA is variable. AMI may be due to atherosclerotic mechanisms (mainly plaque rupture or erosion, or calcified nodule) or non-atherosclerotic mechanisms (vasospasm, spontaneous coronary dissection, or microvascular dysfunction). Among the diagnostic methods that serve to clarify the point is OCT. A recent publication serves to differentiate the prognostic value of the aforementioned mechanisms. It is a single-center study with retrospective analysis of data collected prospectively in a center in China. Between January 2016 and December 2019, 7423 patients were admitted with a diagnosis of AMI and studied with coronary angiography. MINOCA was diagnosed in 294 according to the aforementioned criteria. Of these, 190 underwent OCT. The study could not be performed in patients with complex and tortuous coronary anatomy, renal dysfunction, or hemodynamically unstable. Of the 190 patients with OCT, 99 (52%) were diagnosed with atherosclerotic mechanisms responsible: plaque erosion in 64 (33.7%), rupture in 33 (17.4%), and calcified nodule in 2 (1.1%). Non-atherosclerotic mechanisms were diagnosed in the remaining 91 patients (48%): dissection in 8 (4.2%), spasm in 9 (4.7%), and the cause could not be classified in 74 (38.9%). Compared with their counterparts, patients with atherosclerotic mechanisms were more frequently men, smokers, with ST-segment elevation AMI and higher troponin values. In them, the presence of arteries with <30% lesion was less frequent, and the finding of arteries with lesions between 30 and 50% was more prevalent. Regarding the lesions considered to be responsible for the condition, in the cases of atherosclerotic mechanism the area of stenosis was larger, the lesions were longer, the fibrous cover of the plaques was thinner, and the lipid content was higher. Thrombus was observed in 86% of patients with an atherosclerotic mechanism and in none of the others. These differences were replicated in the non-culprit arteries.

Follow-up data were available for 187 patients at a median of 720 days. In the first year, patients with atherosclerotic mechanisms experienced 15 major cardiovascular adverse events (15.3%): 2 cardiac deaths (2%), 6 culprit lesion revascularization procedures (6.1%), 1 ischemic stroke (1 %) and 6 readmissions for progressive angina (6.1%). Patients with non-atherosclerotic mechanisms experienced only 4 major cardiovascular adverse events (4.5%): 3 cardiac deaths (3.4%) and 1 non-fatal AMI (1.1%), all in patients with a cause not specified by the OCT.

These two publications contribute to unraveling the causal mechanisms and strengthening a diagnostic strategy in the field of AMI with non-obstructive coronary artery disease. The first is a large meta-analysis. The diagnosis of MINOCA is of increasing incidence. This is mainly due to 2 conditions: the expansion of the use of troponin as a diagnostic tool, which leads to increased detection, and a greater awareness of its relevance and prognostic significance. The almost systematic performance of coronary angiography in the presence of an increase in troponin and a compatible condition leads to a more frequent diagnosis of this type of condition. At the same time, the use of CMR is growing as a study that makes it possible to define precise patents to differentiate ischemic and non-ischemic conditions when doubts about the coronary origin persist. One merit of this meta-analysis is that it included only studies in which CMR was performed within the first 10 days, thus avoiding the loss of sensitivity that occurs when carrying out the studies late, when the initial findings fade. It is relevant to take into account some findings. First, that MINOCA was confirmed in only one fifth of the cases; this confirms the criterion of the concept of "working diagnosis" and reveals how close in their presentation are pictures of different etiology and pathophysiology. It is true that when coronary angiography accurately indicates the image of a <50% lesion that seems to be responsible for the episode, other studies often do not advance; so it is possible that many MINOCAs have not then reached CMR, which dilutes their prevalence. within the compatible boxes. Second, the reaffirmation that MINOCA is not a trivial condition: compared to myocarditis and Takotsubo, it is associated with a worse prognosis, so an accurate initial diagnosis is essential to implement measures that contribute to improving evolution in time and prevent future events. Third, that in this line it is regrettable that almost a third of the cases remained undiagnosed; the publication does not clarify the prognosis for this group, who had symptoms compatible with AMI and whose mechanism was unknown (it is not innocuous to have troponin elevation). Fourth, the idea of supporting CMR as a central diagnostic method seems attractive: the information it provides is extremely rich; but let us take into account this third of undiagnosed patients, the high heterogeneity between the publications on the proportion of each of the diagnoses out of the total (for example, the 95% CI of normal findings ranges from 18% to 38%) and the limitations on the availability of the resource in many media. If we have CMR, its use in cases like these seems indicated, although it does not provide absolute certainty in all cases; if we do not have it, we must use all the means at our disposal to clarify the responsible mechanism. It is not of little importance to thoroughly review the initial coronary angiography: more than once the repeated examination allows to detect thrombi, dissections, lesions, unnoticed in the first observation.

The second study follows the same line as the previous one, in this case using a less widespread diagnostic method in our setting, OCT. It focuses on patients in whom the diagnosis of MINOCA has already been made (myocarditis, Takotsubo, etc. have already been excluded). Atherosclerotic and non-atherosclerotic mechanisms appear equally distributed. Logically, pictures of atherosclerotic origin share clinical and pathophysiological characteristics with traditional obstructive coronary disease: a higher prevalence of men, smokers, ST-segment elevation

AMI, plaques rich in lipids and with a thin coating, more predisposed to rupture, thrombosis. Although by definition they are <50%, the presence of lesions between 30% and 50% is higher in this group. It seems that in these patients there is simply a question of degree with obstructive coronary artery disease. On the other hand, what generates more doubts is the counterpart of patients in whom a non-atherosclerotic mechanism is diagnosed. Perhaps the term "diagnostic" is too ambitious: it can only be affirmed that there is no demonstration of the phenomena of the previous group in the OCT, but in 74 of the 91, more than 80%, there is no defined mechanism that has led to the MINOCA, and this is striking. The lack of systematic CMR raises a question: are there not clinical entities among these patients that this study would have contributed to diagnose? Are all these patients truly MINOCA? The authors maintain that in half of these cases, characteristics of the angiographic study suggested microvascular disease; even so, more than 30 patients remain in the nebula. And to be honest, there is a previous doubt: of the 294 initial patients, in more than a third the OCT was not carried out. It is not explicit why, nor if these patients had differential characteristics, which makes the conclusions of the study somewhat less certain. What is clear is that the presence of atherosclerotic mechanisms indicates a worse prognosis, and that the not so fearsome evolution of MINOCA that has been cited so many times is probably the expression of a mixture of patients with different processes involved. In this sense, the pathophysiological information provided by OCT is notable, as well as the limitation for its use in daily practice for logistical and access reasons.

One last comment: the 74 patients without a definite diagnosis with OCT, 38% of the total, remind us of the 27% of CMR with normal findings from the previous study: each method has its limitations. It seems that more than one diagnostic resource is necessary for an accurate definition. We repeat, going back to see the initial coronary angiography in detail should be the rule.

How fast does aortic stenosis progress? Revealing data from a meta-analysis

Willner N, Prosperi-Porta G, Lau L, Nam Fu AY, Boczar K, Poulin A et al. Aortic Stenosis Progression: A Systematic Review and Meta-Analysis. **JACC Cardiovasc Imaging 2023;16:314-28. https://doi.org/10.1016/j.jcmg.2022.10.009.**

Aortic stenosis (AS) is the most prevalent valve disease in the West. Its prevalence increases with age, and when it reaches severity criteria, the only therapeutic solution is valve replacement, surgical or percutaneous. A common problem that arises in daily practice is being able to predict, when faced with a patient with mild or moderate AS, in what time it will become severe. The information in this regard is scattered and sometimes contradictory. The question has become more important since randomized studies have indicated that invasive treatment is associated with a better prognosis in advanced conditions regardless of the presence of symptoms.

In this sense, the publication of a systematic review and meta-analysis of prospective studies with follow-up of at least 12 months in which the severity of the disease and its annual progression were evaluated in patients with AS, with the use of echocardiographic parameters, is extremely useful: mean gradient (MG), peak gradient (PG), peak velocity (PV), or aortic valve area (AVA); or computed tomography, with determination of a valve calcification *score*.

After an exhaustive selection process, 24 studies with 5450 patients, with mean age 68 years, 60% men, were considered for analysis. Mild AS was defined as that with a MG < 20 mm Hg, a PG < 36 mm Hg, a PV of 2.5-3 m/s, or an AVA > 1.5 cm^2; as moderate AS, those with MG 20-40 mm Hg, PG 36-64 mm Hg, PV 3-4 m/s or an AVA 1-1.5 cm^2 ; and as severe AS, those with MG > 40 mm Hg, PG > 64 mm Hg, PV > 4 m/s or AVA < 1 cm^2 . Regarding valve calcification, mild AS was considered if the calcium *score* was <500 AU, moderate AS with values between 500 and 1500, and severe AS with values >1500 AU.

When considering MG as the baseline parameter to classify the severity of AS, a mean rate (95% CI) of annual progression of said parameter of 2.3 (0.9-3.7) mm Hg was observed in mild AS, 4.3 (3.2-5.7) mm Hg in moderate AS and 10 (9-11) mm Hg in severe AS (p<0.001 for the difference in progression according to baseline severity, although with high heterogeneity in the results).

Considering PV as the baseline parameter, the average rate (95% CI) of annual progression of this parameter was 0.09 (-0.04-0.21) m/s in mild AS; 0.18 (0.12-0.23) m/s in moderate AS and 0.33 (0.21-0.46) m/s in severe AS (p=0.001 for the difference in progression according to basal severity, although also with high heterogeneity).

In the case of the PG, the annual changes were respectively 5.7 (0.09-11.3) mm Hg, 6.6 (5-8.3) mm Hg and 15 (12-17.9) mm Hg. The heterogeneity was high, but no significant difference could be demonstrated according to baseline severity, due to the similarity of progression between the mild and moderate forms.

Something similar happened in the case of AVA: the annual fall was almost identical between mild and moderate AS: -0.07 (-0.10 to -0.05) cm^2 and -0.08 (-0.10 to -0.06) cm^2 and higher in severe AS: -0.12 (-0.16 to -0.07) cm^2 .

Regarding the calcium score, there was a significant difference according to the baseline severity of AS, with mean annual increases of 101, 202, and 323 AU in mild, moderate, and severe AS.

The results of this meta-analysis have practical utility. They indicate the expected rate of progression for each parameter of hemodynamic or anatomical severity of AS, according to its severity at the time of the initial examination. It is clear that the most challenging clinical problem we face on a daily basis in this regard is the

time it can take for moderate AS to progress to severe AS. In this sense, considering the upper end of the 95% CI for gradients and speed, and the lower end for AVA (which implies the greatest drop), we can estimate this time. For example, in the case of PV, in moderate AS the upper end of the 95% CI in the annual rate of progression is 0.23 m/s. Getting from 3 m/s (moderate AS) to 4.1 m/s (severe AS) can take a minimum of almost 5 years: (4.1-3) /0.23. Of course, these data are estimates: they are a summary measure of change, summarizing the information from large numbers of individual patients into a single number. Individual baseline characteristics are not taken into account. For example, in a patient with chronic kidney disease in advanced stages, with an increased incidence of calcification processes, the times are surely shortened substantially.

In the case of echocardiographic parameters, it is noteworthy that only the rate of progression of MG and PV is different depending on the initial severity. The authors maintain that this is due to the fact that the calculation of the PG amplifies the error that may have occurred in the measurement of the PV, since PG=4 (PV)² ; and that the determination of the AVA (although essential when defining the severity of the AS) is subject to methodological issues that may vary according to the operator and the technique. In any case, the high heterogeneity of the findings in each of the parameters explored should be highlighted, which makes the summary value more of a global expression than a determination that we can apply with absolute certainty. The final message is perhaps something that we intuitively apply in daily practice: the closer a condition is to advanced stages that require taking extraordinary measures, the closer follow-up and more frequent diagnostic studies should be implemented.

Meta-analysis of TAVI vs Surgical Valve Replacement: Differences in Outcomes by Baseline Risk in Randomized Trials

Ahmad Y, Howard JP, Arnold AD, Madhavan MV, Cook CM, Alu M et al. Transcatheter versus surgical aortic valve replacement in lower-risk and higher-risk patients: a meta-analysis of randomized trials. **Eur Heart J 2023;44:836-52. https://doi.org/10.1093/eurheartj/ehac642.**

Since its inception, transcatheter aortic valve implantation (TAVI) has played an increasing role in the treatment of severe AS. Initially tested in inoperable patients vs. medical treatment was later compared with surgical valve replacement (SAVR) in high-risk surgical patients, and then in lower-risk patients. The demonstration of non-inferiority with respect to SAVR, with shorter hospitalization times and a reduction in a series of complications, gave TAVI a clear place in the treatment of AS. As with any new technology, the necessary learning curve, and cost and effectiveness issues also influence the decision to go ahead. An objection usually made is related to the follow-up time of the studies, often judged insufficient to define durability of the implant and long-term results.

We are now aware of a meta-analysis that considered only randomized studies (excluding observational studies) that compared TAVI with SAVR, with a minimum follow-up of 1 year. It has the virtue of incorporating the maximum follow-up reported so far from each study. The main outcomes were all-cause mortality, all strokes, and the composite of death or disabling stroke, as reported in each trial. Secondary endpoints included cardiac (or cardiovascular) death, disabling stroke, AMI, permanent new pacemaker implantation, aortic valve reoperation, major bleeding, major vascular complications, paravalvular leak, occurrence of atrial fibrillation (AF), rehospitalization and the incidence of acute kidney injury (AKI)

Eight studies were included, divided by the baseline risk of the patients, according to the STS-PROM *score* (Society of Thoracic Surgeons score for predicting mortality) into low- and high-risk studies. For each study, subsequent publications to the original that updated data on long-term survival were also considered. Low-risk studies were those with an STS-PROM score < 4%: PARTNER 3, Evolut Low-Risk, NOTION, and UK TAVI. The mean age in these studies ranged from 73 to 81 years. High-risk studies (STS-PROM > 4%) were PARTNER 1A, CoreValve High-Risk, PARTNER 2, and SURTAVI. The mean age in this case ranged from 79.8 to 84 years. In total, 8698 patients were treated, 3557 low risk, 5141 high risk; 4443 assigned to TAVI and 4255 to SAVR. The maximum duration of follow-up available for this analysis was 1 year in one trial, 2 years in two trials, 5 years in four trials, and 8 years in one trial. The weighted mean duration of follow-up was almost 4 years, 46.5 months. The risk ratio for early events (within the first year of follow-up) between TAVI and SAVR was expressed as RR, and after the first year and globally as HR, in both cases with their corresponding 95% CI.

When considering death from all causes as the endpoint, in the four low-risk studies, the RR with TAVI compared to SAVR within the first year was 0.67 (95%CI 0.47-0.96), p=0, 03. At longer-term follow-up, the HR was 0.90 (95% CI 0.69-1.17), p=NS. Assessing total follow-up duration with a meta-analysis of reconstructed individual data, there was no significant difference, but a trend, in all-cause mortality between TAVI and SAVR (overall HR 0.79, 95% CI 0.60–1.04, p = 0.09), with significant heterogeneity in the results, and with a difference in mean survival between the two strategies of only 0.8 months, not significant: 54.3 vs 53.5 months. In the four highest-risk trials, the RR within the first year was 0.93 (95% CI 0.81–1.08), and the longer-term HR was 1.04 (95% CI 0.96–1.13), in both cases with p=NS. In these trials the proportional hazards changed over time. There was a lower risk of death with TAVI up to 6 months (HR 0.68, 95%CI 0.56-0.82, p<0.01), but higher risk beyond 6 months (HR 1.17, 95% CI 1.05-1.29, p<0.01). When evaluating

the total duration of follow-up, there was no difference between the two groups (OR 1.07, 95% CI 0.95-1.20, p= 0.27), with a difference in mean survival of only 0.5 months, not significant (46.2 vs. 45.7 months).

Regarding the stroke endpoint, in the four low-risk trials, the RR of TAVI relative to SAVR was 0.91 (95% CI 0.46-1.80), and at longer follow-up term, the HR was 0.93 (95% CI 0.66–1.31), in both cases with p=NS. In the four highest-risk trials, the situation was analogous: the RR at one year was 0.93 (95%CI 0.68-1.27), and the HR after one year was 0.94 (95%CI 0.75-1.18), also with p=NS in both cases. When evaluating the total follow-up duration for each trial as a whole with the meta-analysis of reconstructed individual data, there was a lower risk of stroke with TAVI up to 3 months for the low-risk studies (HR 0.52, 95% CI 0 0.30-0.88) but higher risk later (HR 2.14, 95% CI 1.22-3.78), without significant differences when evaluating global follow-up (OR 1.03, 95% CI 0.71- 1.49, P = 0.87). For the high-risk trials, there was no difference in stroke risk up to 3 months (HR 0.87, 95% CI 0.68–1.12) and thereafter (HR 1.06, 95% CI 0.82-1.37).

The composite endpoint death or disabling stroke reproduced the trends indicated when talking about all-cause mortality. In low-risk studies, the RR up to one year was 0.68 (95% CI 0.50-0.92), p=0.01; and the HR after one year 0.85 (95% CI 0.63-1.15), p=NS. Overall, the HR was 0.85 (95% CI 0.67-1.08). In high-risk studies, the RR after one year was 0.90 (95% CI 0.79–1.02) and the HR after one year was 1.04 (95% CI 0.96–1.13), always with p=NS. When considering the incidence of events at 6 months instead of 1 year, a dual behavior was again seen: at 6 months risk reduction, with HR 0.73 (95% CI 0.62–0.85), p < 0 .01), and then increased risk, with HR 1.20 (95% CI 1.09–1.33), p < 0.01. When evaluating the total duration of follow-up, there was no significant difference between the two groups (OR 1.09, 95% CI: 0.97–1.23, p = 0.12), with a small difference in event-free survival, 44.8 vs. 44.4 months.

Regarding secondary endpoints, assessed up to 1 year of follow-up, in the low-risk studies there was no significant difference between TAVI and SAVR for AMI and valve reoperation. TAVI was associated with increased need for a new permanent pacemaker and mild to moderate paravalvular leak and major vascular complications, but with lower risk of disabling stroke, cardiac death (borderline statistical significance, p=0.05), rehospitalization, AKI, AF and major bleeding. In the higher-risk studies, there was no significant difference between the two strategies for cardiac death, MI, or disabling stroke, but, as in the low-risk studies, greater need for permanent pacemaker, aortic valve reoperation, mild paravalvular leak and moderate and major vascular complications; and reduction of new AF, AKI, or major bleeding.

This meta-analysis offers us the longest follow-up to date, based on all available sources and updates, of the total number of randomized TAVI vs. SAVR studies carried out to date. Initially emerging as a therapeutic alternative in patients with inoperable AS or high surgical risk, the practice of TAVI has been expanding, as is the case with many other treatments, to less serious conditions. Thus, for example, the annual mortality in the PARTNER 1A study in 2011 was 24.2% in the TAVI group and 26.8% in the SAVT group; in the PARTNER 2 study in 2012, 12.3% with TAVI and 12.9% after SAVR; and in the PARTNER 3 trial, in low-risk patients in 2019, 1.0% with TAVI and 2.5% with SAVR.

As relevant results, we can conclude that, in studies with low-risk patients, there is, with TAVI compared to SAVR, a reduction in the risk of death in the first year, and of death plus disabling stroke. Considering only the effect on stroke, a risk reduction is verified only up to 3 months, but it increases afterwards, so the effect after one year is neutral. In extended follow-up, the effect on total mortality is attenuated, and is restricted to a trend. What are also the advantages for TAVI? Less disabling stroke as an individual event, arrhythmias, bleeding, and AF, and a strong downward trend in cardiac mortality. The price to pay? Increased need for valve reoperation, vascular complications, and permanent pacemaker implantation.

What happens in high-risk trials? We see a reduction in the risk of death or death plus disabling stroke only in the first 6 months, with an increase thereafter, so that the final effect after one year is neutral. The effects on secondary points are similar to those in low-risk studies.

Events that occur more frequently after TAVI (paravalvular leak, reoperation, need for permanent pacemaker) impact longer-term prognosis; those with greater frequency after SAVR (bleeding, AF, AKI, disabling stroke) are of greater relevance in the short term. This may explain the initial advantage for TAVI compared to SAVR on total mortality, evident up to 1 year in low-risk trials and only up to 6 months in high-risk trials, in which a rebound effect is then verified, which neutralizes the initial advantage when we extend to the year. Therefore, contrary to the widespread belief that TAVI offers a net benefit in survival compared to SAVR in patients at higher risk, it can be deduced from this analysis that the advantage seems to lie in patients who are not so compromised. And, in any case, the difference in event-free survival between the two treatments never exceeds one month. The statistical significance then seems more striking than the clinical one.

As limitations we can mention that we are dealing with a meta-analysis formulated at the study level, not individual data. The authors refer to "reconstructed individual data": this is a technique that infers information from survival graphs, Kaplan Meier curves; there is no true availability of individual patient data. Something that should be highlighted is the high degree of heterogeneity between the studies (significant differences in many of the results), so the summary measure of effect should be seen as suggestive but not as certainty of the magnitude of a particular effect.

Finally, this meta-analysis is of randomized studies, with all due considerations for high internal valid-

ity and more debatable external validity. Different national and international registries can contribute to a more complete picture of reality, with the inherent risk of the presence of confounders beyond those known. An extension of the follow-up periods of the aforementioned studies, data from new clinical trials and registries will contribute to a more complete knowledge of what we can expect from TAVI in our patients with severe AS in the longer term (further prognosis, implant longevity, etc.) Meanwhile, the development of the technique and its use grow incessantly.

Socioeconomic differences and evolution of AMI in 6 high-income countries

Landon BE, Hatfield LA, Bakx P, Banerjee A, Chen YC, Fu C et al. Differences in Treatment Patterns and Outcomes of Acute Myocardial Infarction for Low- and High-Income Patients in 6 Countries. **JAMA 2023;329:1088-97. https://doi.org/10.1001/jama.2023.1699.**

It is generally recognized that socioeconomic differences translate into a different cardiovascular risk profile of patients, a different degree of coverage, dissimilar access to the health system and use of resources, and, presumably, a different prognosis. It is clear that the evolution of the patients differs between rich and poor countries. But what happens when we focus on rich countries with wide health coverage? Does the socioeconomic level influence the fate of patients? We present a collaborative study conducted in 6 high-income countries: Taiwan, the Netherlands, England, the United States of America, Canada (Ontario and Manitoba), and Israel. This is a retrospective analysis of administrative databases, with the analysis of information on patients 66 years of age or older, hospitalized for an AMI with ST-segment elevation (STEMI) or without ST-segment elevation (NSTEMI). In the case of the United States, these were Medicare patients. The period between the beginning of 2013 and the end of 2018 was analyzed. The data of the patients whose dwelling (defined from the zip code) corresponded to the location of the highest 20% and the lowest 20% of the income distribution were considered in each region. The primary end point was 30-day and 1-year mortality, adjusted for age, sex, and comorbidities; and secondary end points the use of coronary angiography, and the performance of angioplasty and coronary surgery. Patients who had had an AMI in the year prior to the index hospitalization were excluded.

A total of 289 376 hospitalizations for STEMI and 843 046 with NSTEMI were analyzed. The income ratio between rich and poor patients ranged from 1.35 in Taiwan to 4.36 in Israel. The incidence of both AMI types was higher among the lowest-income patients in all 6 countries; the most striking differences were seen in Israel, with annual STEMI incidence of 2.1 ‰ in the poorest 20‰ and 1.1 ‰ in the richest 20%, and corresponding figures of 4.8 ‰ and 2.3 ‰ for NSTEMI. The incidence of hard events was higher among the poor. With regard to STEMI, the most notable difference in 30-day mortality was seen in Canada (2.9% excess), while in Taiwan it was practically nil; in mortality at one year, the greatest excess mortality among those with lower incomes was seen in Israel (9.1%), while in Taiwan again it was around 0. Regarding NSTEMI, in 30-day mortality the most notable difference was seen in Israel (2.8% excess among the poor) and something similar occurred at 1 year (6.7% excess) while in Taiwan there were no significant differences between poor and rich at 30 days or 1 year.

For cardiac catheterization, the utilization rate was also higher among wealthier patients in all cases, with the greatest difference in England (5.9% excess in STEMI and 9.6% in NSTEMI). , and the lowest in Taiwan (2.4% and 1.7% respectively). And for coronary angioplasty, again the biggest difference was seen in England (6.1% and 6.5% for STEMI and NSTEMI) and the smallest in the Netherlands for STEMI (3.3%). and in Taiwan for NSTEMI (1.6%). The length of stay was shorter for wealthier patients, except in Israel and Taiwan, and the 30-day readmission rate was also lower for higher-income patients.

This analysis delivers a series of interesting conclusions. Even in rich countries with good health systems, socioeconomic differences appear to be associated with different rates of resource utilization and evolution of AMI in different socioeconomic strata. It is nonetheless interesting that the country with the least inequality (Taiwan) appears as the one with no difference in mortality from AMI at 30 days and one year; and that the country with the greatest difference in income between rich and poor (Israel) is the one with the greatest difference in mortality for STEMI at one year, and for NSTEMI at 30 days and one year. There is, it is true, no absolute correspondence between the differences in the indication for catheterization and angioplasty and the differences in mortality: England appears as the country with the greatest discrepancy in the use of catheterization and angioplasty between rich and poor for both types of AMI, but it is not for this is the one with the greatest difference in mortality (even for STEMI it is in fourth place among the 6 considered). The poor not only have higher mortality in general: their length of stay time is longer, and their readmission rate is higher, in all countries. This suggests that other factors, beyond revascularization, influence the long-term prognosis. Despite adjusting for age and comorbidities, other factors undoubtedly play a role. And in this sense, it is regrettable that this analysis does not consider, for example, the differences in outpatient drug treatment. We do not have data on antiplatelet drugs, statins, and neurohormonal antagonists; surely part of the differences in the prognosis of the patients go beyond what happens to them in hospitalization: complete medical treatment, frequency of follow-up visits, easier access to the consultation, adequate compliance with diet, recreation and physical activity, are all factors that we know differ between poor and rich and undoubtedly also define their prognosis..